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13. ABSTRACT (Maximum 200 words) Cognitive and psychomotor performance and mood states, including many critical behavioral functions such as sleep, memory, reasoning, and vigilance, are significantly impaired by ascent to HTE higher than 3,000 m. Impairments in behavior caused by HTE can degrade military operations because the judgment and rate and accuracy of performance of military personnel can be affected. Such adverse effects have distinct and measurable time courses; onset of some effects is immediate (cognitive performance), whereas the onset of others is delayed (symptoms of AMS or adverse moods). The behavioral consequences of HTE are primarily dependent on the level of altitude, the duration of exposure the rate of ascent, an individual's state of physiological acclimation or acclimatization, characteristics of the task performed, and characteristics of the individual such as hypoxic sensitivity. Military history documents that the adverse effects induced by HTE need to be considered when military operations at altitude are planned and undertaken. Current research indicates that some performance decrements induced by ascent to extremely high mountains (e.g., Mount Everest, 8,848 m) may persist for a year or longer after return to lower elevations. Psychological, operational, and medical strategies have been employed to minimize these adverse effects. Psychological strategies often involve training and familiarization with the adverse effects that will be experienced at high altitude. Operational strategies include staging at intermediate altitudes, acclimatizing, and using supplemental oxygen from tanks of oxygen generators. Medical strategies often involve the use of medications to improve functioning at altitude and techniques to avoid complications. In most situations, multiple strategies are employed. The strategies now available and new developments to come will ensure that high-altitude military operations in the future will be less affected by adverse changes in cognitive and psychomotor performance and mood.				
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# Chapter 23

## COGNITIVE PERFORMANCE, MOOD, AND NEUROLOGICAL STATUS AT HIGH TERRESTRIAL ELEVATION

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### INTRODUCTION

#### SELECTED SYSTEMS OR PROCESSES AFFECTED BY EXPOSURE TO HIGH TERRESTRIAL ELEVATION

- Mobility and Mission Accomplishment
- Mood States
- Personality
- Cognitive and Psychomotor Performance
- Vision, Hearing, and Taste
- Speech
- Sleep
- Neuronal Cells
- Neurochemical Mechanisms
- Changes in the P300 Waveform

#### VARIABLES THAT INFLUENCE EFFECTS AT HIGH TERRESTRIAL ELEVATION

- Threshold Altitude for Effects
- Time Course of Effects
- Temporary Versus Long-Term Effects
- Cognitive Task Complexity and Practice
- Individual Differences
- Performance Tradeoffs of Speed Versus Accuracy
- Correlations Between Measured Effects

#### COPING WITH HIGH TERRESTRIAL ELEVATION AND MINIMIZING ADVERSE EFFECTS

- Psychological Strategies
- Operational Strategies
- Medical Strategies

### SUMMARY

### DISTRIBUTION STATEMENT A

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## INTRODUCTION

Many military, recreational, and industrial settings expose people to the effects of high terrestrial elevation (HTE). Such high-altitude environments (ie, 3,000–8,848 m) often involve risk; moreover, the consequences of faulty judgment or a cognitive error can be deadly or costly. Some of the earliest information about the psychological effects of HTE came from people working or living in high mountainous regions or people exploring conditions involving hypoxia.<sup>1,2</sup> Regions at high elevations are often important for military, economic, geopolitical, and other reasons.

High ground is usually sought during military operations.<sup>3,4</sup> High terrestrial elevations offer advantageous sites for observation and grant the holder the strategic advantage in that area. Hence the military was interested in balloons and explored their feasibility for observation and scouting in the late 1700s.<sup>1,2,5</sup> In the late 1960s, analyses of military history were published that showed that combat units that resided at altitudes higher than 3,000 m for a few days before engaging in warfare at even higher altitude (eg, 4,000 m) gained a dramatic advantage.<sup>6,7</sup> In contrast, unacclimatized troops coming immediately from positions near sea level experienced the rigors of the terrain, the liabilities of acute mountain sickness (AMS), and an adversary who was already emplaced.

Such effects, and others to be described in this chapter, result because above 3,000 m the substantially reduced atmospheric pressure associated with HTE causes hypoxemia (inadequate oxygenation of the blood), because the lungs cannot extract sufficient oxygen. The importance of oxygen for normal functioning and survival is emphasized by the fact that even at sea level the brain requires a disproportionately large amount of blood (enriched with oxygen) to function normally. Specifically, an adult human brain receives about 15% of the total volume of blood pumped by the heart, whereas the brain is only 2% of the body's weight. Normally, a healthy adult brain consumes 3.3 mL of oxygen per 100 g of brain tissue per minute,<sup>8</sup> which is approximately 20% of the oxygen consumed by the human body under resting conditions.

Hypoxemia results when individuals are exposed to HTE. Hypoxemia also results from procedures that are used to simulate the effects of HTE (eg, exposure to gas mixtures with ~ 13% oxygen, or special environments with atmospheric pressure ~ 70% that at sea level). This chapter will therefore describe findings resulting from exposure to HTE and the use of methods to simulate the effects of HTE.

In the last 100 years, technology has created microenvironments that are of special interest because some make people hypoxemic. Early airplanes, which did not have supplemental oxygen or internal compartment pressurization, made pilots, crews, and passengers hypoxemic.<sup>9–12</sup> Stowaways traveling infrequently in wheel compartments or nonpressurized areas of newer commercial aircraft experienced even more extreme conditions.<sup>13</sup> Surprisingly, sometimes stowaways survived extreme hypoxemia and cold (11,000 m and –65°C) during such flights. Today, another microenvironment that sometimes causes hypoxemia is astronomical observatories at HTE with large telescopes for viewing the galaxies, planets, comets, and stars. Observatories, constructed at altitudes of 4,000 to 5,000 m, provide better views of the solar system because they are above most of the low-altitude haze and pollutants.<sup>14,15</sup> Although observatories at HTE enhance the optics of the telescope, such work sites create new problems for the employees because their bodies and brains are hypoxemic. An important military microenvironment that can cause hypoxemia is the submarine. In some modern submarines, the atmospheric pressure is deliberately reduced so that the risk and destructiveness of fires on board are greatly decreased.<sup>16</sup> Selection of appropriate, reduced atmospheric pressures inside submarines was heavily guided by choosing those that would provide an optimal compromise between the adverse impact on personnel aboard (hypoxemia) while providing reasonable protection against fires.

Today, many land masses at HTE are especially important for military and recreational purposes.<sup>4</sup> Military personnel train for varied high-altitude missions, because mountain passes and flat expanses at high altitude (altiplano) are of great strategic and military importance.<sup>3,4</sup> Phenomena at HTE are also of interest to many civilians because, since 1970, many more have climbed to altitudes above 5,000 m.<sup>17–21</sup> Also, recent trends in climbing dictate that it is fashionable and desirable to climb the highest mountains in the world, often without oxygen, such as Mount Everest (8,848 m). Today, sites at HTE are more accessible than ever before, the climbing equipment and clothing are matchless, and people with minimal experience are attempting Mount Everest and other high mountains.<sup>17,19–21</sup>

This chapter will examine some of the psychological consequences that result from exposure to HTE, such as its effects on our senses, sleep, mood, judgment, memory, and ability to perform cogni-

tive and psychomotor tasks. We will review the minimum altitude for threshold effects and evaluate data that suggest that long-term effects may result from exposure to extreme elevations. Lastly, we

will look at some of the strategies used to reduce the adverse effects of high altitude so that people can function better and experience a greater sense of well-being at HTE.

## **SELECTED SYSTEMS OR PROCESSES AFFECTED BY EXPOSURE TO HIGH TERRESTRIAL ELEVATION**

Exposure to high altitude affects many bodily processes and functions. Moreover, the onset of effects varies from immediate to several days or weeks. In planning military operations at HTE it is important to be able to predict the types, magnitudes, and time courses of impairments that will be experienced. This section describes adverse changes that usually occur after exposure to HTE higher than 4,000 m, such as those in mobility and mission accomplishment, mood states, cognitive and psychomotor performances, the senses, and sleep.

### **Mobility and Mission Accomplishment**

The strenuous demands of a military training exercise in an intermediate high altitude (2,100–3,050 m) and a cold environment have been described aptly by Davis and colleagues<sup>22</sup>:

The high-altitude, snow-covered environment is unique in the demands imposed on marines. Failure to recognize and consider the implications of this environment can drastically distort operational requirements. It is difficult to convey all the encumbrances associated with maintenance of basal tasks in this environment.<sup>22(p37)</sup>

Even at lesser altitudes of 2,065 to 2,620 m, 9 of 638 Marines (1.4%) in a US Marine Corps Battalion Landing Team that was conducting mountainous warfare training experienced incapacitating symptoms (eg, headache, nausea, malaise) of AMS.<sup>23</sup> Considering the exceptional motivation and discipline that is typical of Marine units, it is likely that although some individuals were uncomfortable and affected by the effects of high altitude, they did not seek medical help. The fact that this incidence occurred at altitudes only slightly higher than that of Denver, Colorado, suggests the generality and relevance of this information, because intermediate altitudes such as these are experienced by many military personnel, skiers, novice climbers, and hikers.

Historical data from civilian climbing expeditions have shown that conditions associated with climbing, high altitude, and cold can be life-threatening and sometimes fatal. Even lesser mountains such as Mount McKinley (6,194 m) in Alaska, with

its highly unpredictable and extreme weather, is a foreboding challenge. In 1992, 13 climbers died (a 2- to 6-fold increase over most prior years) while attempting to climb the mountain. Of those who tried to climb Mount McKinley in the first 6 months that year, only 39% succeeded, a percentage much lower than usual. By the end of June 1992, 11 climbers had died; this 6-month total surpassed any previous 12-month total. By contrast, from 1980 to 1992 the median percentage of successful attempts was 51%, and the number of deaths per year averaged 2.5.<sup>20</sup> Although military personnel will be required to go where their mission demands, it is likely that they will be better-trained and -supervised than expeditions undertaken by many civilian climbers, especially those who are novices. The challenges and reputation of Mount Everest are even more fateful. Since the first Western Expedition in 1922, only 600 people have reached the summit, while more than 140 have died in the attempt; in terms of the mission objective, 1 of 7 climbers have reached the summit.<sup>17</sup>

### **Mood States**

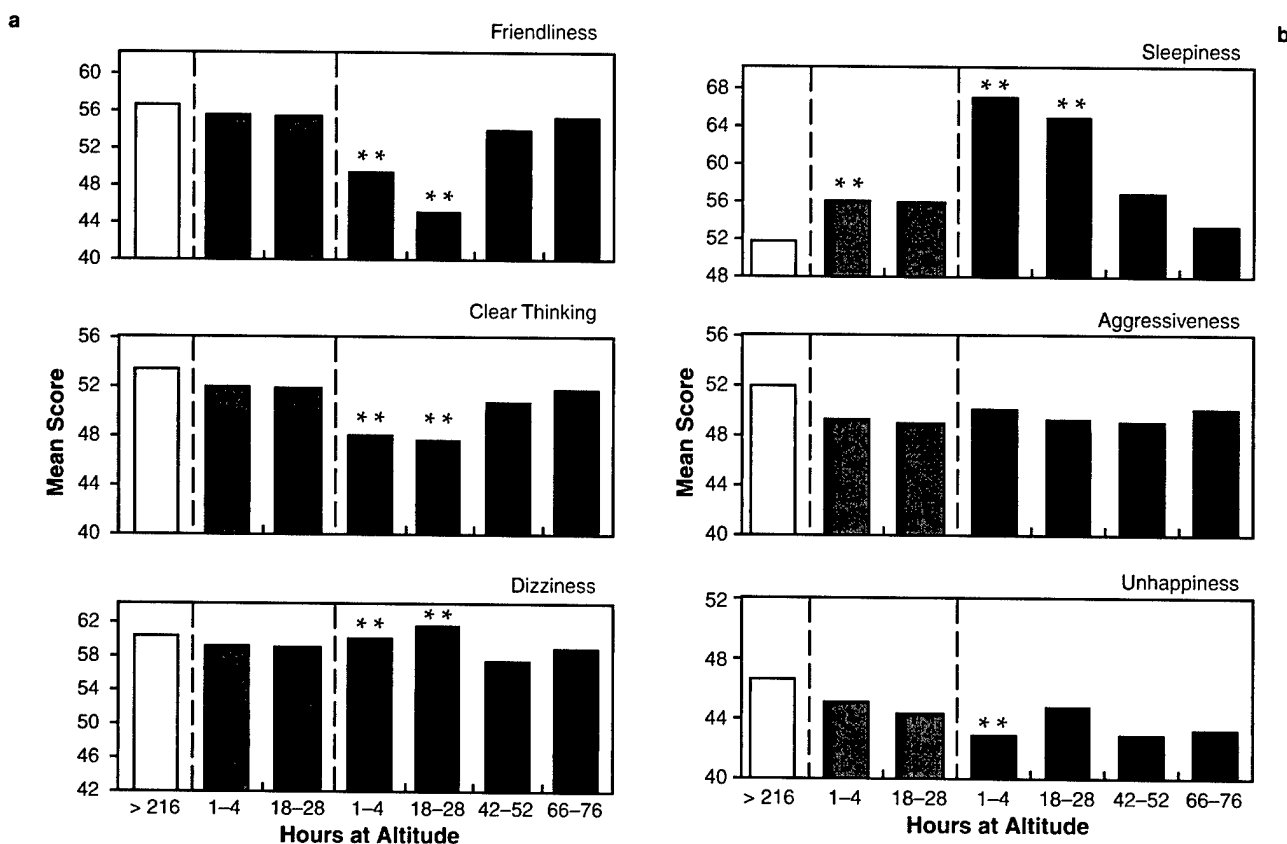
Observed behaviors and personal anecdotes suggest that the initial mood state experienced at altitude is euphoria, followed by depression. Euphoria can lead to dangerous consequences because its effects are usually not recognized by the affected person.<sup>1</sup> With time, individuals may also become quarrelsome, irritable, anxious, and apathetic.<sup>24</sup> At higher altitudes, irritability, not elation, is the more consistent manifestation. Sensitivity to criticism or instruction, aggressiveness, and a free-floating impatience are also more common at higher than at lower altitudes.<sup>25</sup> Overconfidence, often a problem at HTE, occurs frequently with elation and also with an irritable, aggressive mood.<sup>25</sup> Although disturbances in emotional control have been noticed at HTE for decades, until recently there have been few systematic and quantitative studies assessing mood at altitude.

In 1977, Banderet<sup>26</sup> conducted one of the first systematic studies of mood changes at HTE using the Clyde Mood Scale to determine the self-rated moods of volunteers. His effort was part of a larger study

designed to evaluate the efficacy of staging plus acetazolamide (treatment) for the prevention of AMS.<sup>27</sup> Staging involves ascending to one (or more) intermediate altitudes and allowing time for some physiological acclimatization; then, the climber ascends to the summit (or the desired site) at HTE.<sup>1,27,28</sup> Mood states were assessed at 200 m (baseline), 1,600 m (the staging site), and 4,300 m (Pikes Peak, Colo).<sup>26</sup> Mood changes were not observed at 1,600 m, but four of the six mood factors were sensitive to 4,300 m altitude. At 4,300 m, all volunteers (treatment and control groups) rated themselves as less friendly and clear thinking and more sleepy and dizzy than at 200 m. At 4,300 m, the treatment strategy (acetazolamide and staging) resulted in improved mood on the friendly, sleepy, and dizzy factors, but not on the clear-thinking factor. (The characteristics of AMS, its pathophysiology, and its treatment

are described in Chapter 24, Altitude Illness: Acute Mountain Sickness and High-Altitude Cerebral Edema.)

In 1988, Shukitt and Banderet,<sup>29</sup> using the original database of Banderet,<sup>26</sup> compared moods measured with the Clyde Mood Scale at three different altitudes and two times of day (morning and evening) (Figure 23-1). Baseline values were determined at 200 m; moods were then assessed for 2 days at 1,600 m in one group, or for 4 days at 4,300 m with a second group. Only sleepiness changed at 1,600 m; volunteers were sleepier at this altitude compared with sea level. At 4,300 m, moods differed from baseline (200 m) after 1 to 4 hours and differed even more after 18 to 28 hours; volunteers became less friendly, less clear thinking, and dizzier.<sup>29</sup> They also became sleepier and happier, with effects being greatest after 1 to 4 hours. Aggressive-



**Fig. 23-1.** Time courses of varied mood states: (a) friendliness, clear thinking, and dizziness, and (b) sleepiness, aggressiveness, and unhappiness at simulated altitude conditions of 200 m (no shading), 1,600 m (light shading), and 4,300 m (dark shading). Two asterisks atop a bar indicate that the mood state was significantly different ( $P \leq .01$ ) at 4,300 m than at 200 m. Reprinted with permission from Shukitt-Hale B, Lieberman HR. The effect of altitude on cognitive performance and mood states. In: Marriott B, Carlson SJ eds. *Nutritional Needs in Cold and in High-Altitude Environments*. Washington, DC: National Academy Press; 1996: 437.

ness did not change.<sup>29</sup> However, by 42 to 52 hours after ascent to 4,300 m, all moods returned to baseline levels. Mood states each morning and evening were similar at each altitude (1,600 and 4,300 m). Therefore, at 4,300 m, five moods differed from baseline 1 to 4 hours after arrival, three differed even more after 18 to 28 hours, and after 42 to 52 hours all previously affected moods returned to baseline values. Mood states were adversely affected by both duration of exposure and level of altitude (1,600 and 4,300 m); changes in mood states at altitude had a distinct and measurable time course.<sup>29</sup>

In another study, mood states were evaluated using the Profile of Mood States and the Clyde Mood Scale during a 4.5-hour exposure to a simulated altitude of 4,200 or 4,700 m to examine changes as a function of altitude level and duration of exposure.<sup>30</sup> Effects of 4,700 m altitude were seen for 75% of mood factors (friendliness, sleepiness, dizziness, hostility, depression, anxiety, confusion, fatigue, tension, anger, and vigor), while the effects of 4,200 m altitude were seen for only 25% of mood factors (sleepiness, dizziness, tension, and confusion). More adverse changes were noted with longer durations after ascent, especially for 4,700 m simulated altitude. This study, like Banderet's earlier study,<sup>26</sup> demonstrated that moods are significantly altered after only a few hours of exposure to simulated altitude; effects increase (incidence and magnitude) when testing is conducted at 4,700 compared with 4,200 m.<sup>30</sup>

In still another study, Shukitt-Hale, Rauch, and Foutch<sup>31</sup> evaluated self-rated symptoms and mood states during a climb of Mount Sanford in Alaska. Self-rated moods and symptoms were determined with the Profile of Mood States and the Environmental Symptoms Questionnaire.<sup>32-35</sup> In their 1990 study, Shukitt-Hale and colleagues<sup>31</sup> studied seven males for 7 days during a climb to 3,630 m. The volunteers were tested at four increasing altitudes: they were tested twice at 2,225 m and once at 2,530 m, 3,080 m, and 3,630 m. Seven symptom factors and two mood factors were adversely affected by changes in altitude. The volunteers experienced more respiratory AMS, exertion stress, and muscular discomfort, and they were colder, less alert, less vigorous, and more fatigued at the higher altitudes. Fewer adverse effects on day 2 at 2,225 m suggest that some acclimatization may have taken place from day 1 to day 2 at this altitude. It is interesting to note that even though the climb to the moderate altitude of 3,630 m in this study was relatively slow (< 300 m/d), adverse changes at this and lower altitudes were evident. These data demonstrate that

a climb to 3,630 m produces adverse changes in symptomatology and mood states, and that other variables associated with a climb (eg, physical exertion or exercise) can affect these parameters.<sup>15</sup>

## **Personality**

Changes in personality associated with exposure to high altitude were reported by several investigators, including Hertzman, Seitz, and Orlansky,<sup>36</sup> who in 1955 examined the relationship between personality and hypoxia. When their subjects spent 47 to 49 minutes at a simulated altitude of 5,638 m, they showed some loss of emotional control, with a tendency toward emotional disorganization and increased anxiety, followed by a counteracting tendency to become more constrictive.

In a different investigation, three standard personality questionnaires and a Mountain Sickness Anticipation Questionnaire were completed prior to departure to the Himalayas to assess the role of personality and expectations in the development of AMS.<sup>37</sup> The symptomatology of AMS was assessed by clinical interview and by peer review. The severity of AMS and its occurrence were not predicted with these methods and bore no significant relationship to personality. For comparison, daily self-assessment of the signs and symptoms of AMS were also conducted throughout the expedition, using graduated and graphic rating scales. Ratings from these graphical rating scales were found to be unreliable and dependent on personality factors. Therefore, the authors concluded that personality is of no significance in the development of AMS, but that it is important in influencing self-ratings of symptom severity.

Intellectual functioning and changes in personality were examined during a 35-day mountaineering expedition to Mount McKinley.<sup>38</sup> At 3,800 m, these indices varied minimally. However, at 5,000 m, undesirable changes were evident; that is, there was a marked deterioration in cognitive ability, a sharp increase in paranoia and obsessive-compulsiveness, and smaller increases in depression and hostility. While these psychological changes may have resulted from high altitude, the heavy physical demands, enforced intragroup dependence required of mountain climbing, close living quarters, extremely cold temperatures, sensory deprivation, and frequent periods of reduced visual fields may also have affected them.

The effects of chronic hypoxemia on cognition and behavior have been studied in women exposed to high-altitude mountaineering.<sup>39</sup> Neuropsychological

logical tests, psychosocial questionnaires, and physiological questionnaires were given to women before, during, and after a Himalayan climb to 6,248 m. Cognitive functioning remained relatively intact with only two significant decrements, complex abstract reasoning and word-finding ability. Significant changes were found on all psychosocial and physiological questionnaires. High positive affect toward others and anxiety, both high before the climb, declined significantly after the expedition. In contrast to this decreased acceptance of others, subjects' self-ratings of their abilities improved after the expedition (ie, increased self-esteem). Self-perception of cognitive and affective functioning was more related to emotional states and physical symptoms than to actual ability to perform. Anxiety, depression, fatigue, and altitude eroded self-confidence, emphasizing the presence of psychological as well as physiological demands of high-altitude mountaineering.

Ryn<sup>40</sup> also described mental disturbances in climbers that he claims are related to duration of stay and level of altitude. The neurasthenic syndrome was common at 3,000 to 4,000 m and is characterized by fatigability, lack of motivation, feelings of inadequacy, and psychosomatic symptoms. The cyclothymic syndrome occurred at 4,000 to 5,000 m and involved alternating depressed and elevated moods. Acute organic brain syndromes occurred above 7,000 m and resulted from structural or functional defects in the central nervous system (CNS). The climber's personality, the emotional atmosphere associated with climbing, the high degree of risk, and other biological and psychological factors were important in the etiology of such mental disturbances.

### **Cognitive and Psychomotor Performance**

In a review of research literature on high-altitude physiology and medicine, Cudaback<sup>14</sup> included some anecdotal reports of astronomers working at high altitude; he reported that the effects of high altitude on performance are often larger than those recognized either by its victims or their colleagues at the same altitude. He suggested that at 4,000 m most unacclimatized people will lose approximately 20% of their sea level abilities, and some loss may persist even after moderate acclimatization. At least half the people with no acclimatization will suffer some sickness starting a few hours after ascent and lasting a few days. Between 0.1% and 1% of individuals going to 4,000 m HTE will suffer serious illness at some time, and that illness may become

life-threatening if the victim does not descend. Mental performance in unacclimatized people on simple, well-learned tasks was impaired 12% to 28%, and impairments on complex tasks were expected to be larger.

High altitude produces substantial impairments in a number of cognitive performances. Impairments in psychomotor performance, mental skills, reaction time, vigilance, memory, and logical reasoning have been demonstrated at altitudes above 3,000 m.<sup>41,42</sup> Performance changes do not follow the same time course at altitude as do symptoms of AMS or moods; therefore, with time, performance will often be affected differently than symptoms or many moods.<sup>43-45</sup> Cognitive performance is usually more vulnerable to altitude than psychomotor performance,<sup>14,28,46</sup> and complex tasks are typically affected before simple tasks.<sup>14</sup> Additionally, activities requiring decisions and strategies are more vulnerable than automatic processes.<sup>47</sup> Deficits of learning and retention of information in perceptual and memory tasks were measured in climbers; climbers also performed more slowly on most tasks than did a control group.<sup>48</sup> (See Exhibit 19-1 in Chapter 19, *Mountains and Military Medicine: An Overview*, for definitions of climbers and other categories of people who visit mountains.) Motivation and training may compensate for the degradation in performance imposed by high altitude.<sup>49</sup>

In 1937, McFarland,<sup>50</sup> in a classic study of the behavioral effects of exposure to HTE conditions, found decrements on several measures of cognitive performance. In 1948, Russell<sup>51</sup> exposed 244 volunteers to simulated altitude (5,486 m) for 35 minutes and measured finger dexterity, arm-hand coordination, and simple addition. Decrement in performance appeared immediately after the introduction to hypoxia, rapid adjustment occurred as the duration of hypoxia increased, and continued practice under hypoxic conditions resulted in improvement. Other investigations have found decrements above 3,000 m in psychomotor performance,<sup>52</sup> problem solving,<sup>53</sup> symbol substitution,<sup>54</sup> card sorting,<sup>55</sup> reaction time,<sup>56,57</sup> vigilance performance,<sup>58</sup> and rifle marksmanship.<sup>59,60</sup>

In 1989, Kennedy and colleagues<sup>61</sup> investigated cognitive function at simulated altitude in a repeated-measures study of performance of seven volunteers; the atmospheric pressure in their chamber was systematically reduced for 40 days to a final altitude equivalent of 8,848 m, the height of Mount Everest (Operation Everest II). Significant impairments in cognitive function were seen for three of the five tests in the computerized test bat-

tery (Sternberg, pattern comparison, grammatical reasoning), and on two paper-and-pencil tests (grammatical reasoning and pattern comparison), every volunteer showed a substantial decrement at 7,625 m. Another study,<sup>62</sup> actually conducted on Mount Everest at altitudes above 6,400 m, showed no reliable effect on the retrieval of general information from memory, and this robustness of retrieval occurred for both recall and forced-choice recognition. However, extreme altitude did affect metacognition (ie, the monitoring and control of one's own cognitive processes); climbers showed a decline in their feeling of knowing, both while at altitude and 1 week after returning from altitude. This study demonstrated that exposures to extreme altitudes produced a decline in feelings of knowing, although there was no change in retrieval as assessed by accuracy of recall, latency of recall, and accuracy of recognition.

In 1985, Forster<sup>63</sup> studied two groups of sea-level residents at the summit of Mauna Kea (4,200 m) in Hawaii to examine the effect of different ascent profiles on performance. People in both groups ascended the mountain in a vehicle. "Commuters" spent 6 hours at the summit, while "shift workers" resided on the mountain for 5 days. Commuters experienced fewer symptoms of altitude sickness than shift workers on the first day at 4,200 m. After 5 days, shift workers reported fewer symptoms and performed better at tests of numerate memory and psychomotor ability than commuters. Therefore, the impairments in cognition at altitudes of 4,200 m are moderate but short-lived when individuals stay at HTE continuously.

In 1991, Koller and colleagues<sup>64</sup> found a 20% increase in errors on a test of mental arithmetic in 7 nonacclimatized subjects during stepwise, acute ascent to 6,000 m, compared with an error rate of about 7% in 10 acclimatized subjects. Because human cognitive function is sensitive to changes in oxygen availability, exposure to hypoxia should produce a continuum of effects as either the level of HTE or the duration of exposure is increased. In a laboratory study, Shukitt-Hale and colleagues<sup>30</sup> evaluated the behavioral effects of hypoxia as a function of duration of exposure and altitude level with various standardized tests of cognitive performance. Each test was administered from one to three times to participants in an altitude chamber during 4.5-hour exposures to three levels of simulated altitude: 500 m (the baseline); 4,200 m; and 4,700 m. A number of measures were affected during the first administration of the tests (after 90 min of exposure). Cognitive performance was signifi-

cantly impaired on 7 of 10 performance measures at 4,700 m; whereas only 4 of 10 measures were affected at 4,200 m. When the results for 4,200 m and 4,700 m were compared, even relatively simple performance tasks (simple and choice reaction time), as well as complex tests of cognition (addition test), resulted in graded impairments. The number of hits on the Bakan vigilance task decreased with increasing altitude, simple reaction time increased as a function of increased altitude, and percentage errors increased on the four-choice reaction time test. The number of correct responses (a measure reflecting both the speed and accuracy of performance) decreased on the addition, coding, number comparison, and pattern recognition with increasing altitude and duration at altitude. Therefore, adverse changes in cognitive performance appeared within 90 minutes of exposure to altitude and were greater with higher altitudes and longer durations (< 4.5 h).

Therefore, it is generally accepted that hypoxia has few effects on human performance at altitudes lower than 3,000 m. Higher than 3,000 m, however, substantial impairments occur in cognitive performance, such as mental skills, reaction time, vigilance, memory, and logical reasoning.

### **Vision, Hearing, and Taste**

Himalayan climbers often report visual and auditory hallucinations.<sup>65</sup> Usually, the senses are affected by altitude before cognitive and psychomotor performances.<sup>42</sup> Temporary visual changes are uncommon but can include blurred vision, flashing lights, blindness, or double vision.<sup>66</sup> Retinal hemorrhages can also occur above 3,600 m; they rarely cause symptoms and heal rapidly.<sup>66</sup> McFarland<sup>12</sup> gives estimates for the loss of function for visual parameters at 4,300 m: 10% in central field extent, 30% in central brightness contrast, 34% in dark adaptation, and 36% in central acuity. Adverse effects on vision may be partially responsible for some of the cognitive performance decrements seen at altitude.<sup>12</sup> As examples, the latencies to read briefly displayed visual stimuli increased with hypoxia,<sup>67</sup> latencies to detect visual stimuli increased with hypoxia,<sup>68</sup> and the detection of signals decreased as the perceptual sensitivity of the visual system changed.<sup>58</sup>

Vision is the first sense affected by hypoxia, with some effects seen at altitudes as low as 1,220 to 1,520 m.<sup>12</sup> Sensitivity to light, visual acuity, and color discrimination decreased at altitudes higher than 3,000 m. Night vision and dark adaptation are particularly sensitive to the effects of hypoxia, because retinal rods and cones are impaired in their ability to



adapt to the dark.<sup>69</sup> Kobrick and colleagues<sup>70</sup> found a continued impairment of night vision (dark adaptation) that prevailed during sustained hypoxia (16 d at 4,300 m) but that recovered substantially when hypoxia was reduced (but not eliminated). They demonstrated that such visual impairments may persist after recovery from symptoms, adverse moods, and impaired performances.<sup>70</sup> Another study<sup>71</sup> found that visual acuity in 11 male and 6 female pilots using the Aviator Night Vision Imaging System (ANVIS) was degraded slightly after 30 minutes of exposure to 4,300 m, although less than what would be expected with unaided night vision under these conditions. There were no visual effects attributable to gender.<sup>71</sup> Therefore, ANVIS might limit degradation of visual performance resulting from hypoxia under low illumination conditions.

Auditory thresholds for different frequencies of sound were relatively insensitive to hypoxia, with few or no changes at HTE as high as 4,600 m.<sup>24,72</sup> Recently, this belief has been challenged by several investigators<sup>73-75</sup> who believe that audition may be more sensitive to hypoxia than previously believed. Although there was a drop in speech discrimination under hypoxia, no significant deterioration in hearing for pure tones was found for 4,600- and 6,100-m conditions in a chamber.<sup>76</sup> The changes in speech discrimination were thought to be due to either lack of oxygen in the cochlea or inattention caused by hypoxia.<sup>76</sup>

The four basic tastes of salt, sour, bitter, and sweet become less pronounced after ascent to moderate altitude, although the appetite for sweet foods is said to increase.<sup>28</sup> This change in taste sensation may be a factor in high-altitude anorexia, a self-induced starvation.<sup>42</sup> Animals<sup>77</sup> and humans<sup>78</sup> lose body weight when exposed to high-altitude conditions, due to reduced daily food intake and perhaps other factors. One study<sup>78</sup> found that hypoxia was associated with an 8.9% reduction in initial body weight, with appetite suppression and decreased caloric intake lasting for several weeks (during the study), particularly due to a decrease in carbohydrate preference, despite access to ample varieties and quantities of highly palatable foods.

## Speech

Some nonperceptible characteristics of speech appear to change after exposure to HTE. Lieberman and colleagues<sup>79,80</sup> reported an innovative and promising methodology that they used to measure small but important changes in speech from five male climbers during the 1993 Sagarmatha Expedi-

tion of Mount Everest. They measured a time interval associated with selective speech sounds, which they called the "voice onset time" (VOT). In normal communications, separation intervals for VOT for "voiced" and "unvoiced" consonants differ by 20 milliseconds or more, so that the sounds from the two types of consonants are distinctive and discernible to a human listener.

Values of the VOT were determined at different altitudes from each climber's speech utterances when he read a list of monosyllabic words. The list contained words like "bat" and "kid," which had voiced and unvoiced consonants at the beginning and end of each word, respectively. These measurements were determined at 5,300 m (the base camp), 6,300 m, 7,150 m, 8,000 m, and on return to 5,300 m. As the climbers ascended to each test altitude, they communicated the standard words on the list to the experimenters (at the base camp). During each test session, the experimenter recorded the climbers' verbalizations for subsequent analysis.

Exposure to high altitude changed the VOTs. The separation interval between voiced and unvoiced consonants changed from 24.0 to 5.4 milliseconds.<sup>79,80</sup> This suggests that it would be more difficult to understand and process verbal communications at high altitude because stop consonants may not be readily perceived. Lieberman and colleagues<sup>79,80</sup> inferred that this change in speech results from the effects of hypoxia on subcortical pathways to the prefrontal cortex.

A second test used by these investigators measured the time required for each climber to process simple and complex sentences; the sentences that were used could be processed easily by a 10-year-old, fluent in the English language.<sup>79,80</sup> Each climber looked at a small booklet with three illustrations per page that reflected various interpretations of a simple or a complex sentence. Before each sentence, the climber announced the number of the page he was viewing; this provided a start event for each reaction time and ensured that the pages in the booklets were synchronized for the climber on the mountain and the experimenter at the base camp. The experimenter read the sentence and the climber verbalized the letter of the alternative he thought was correct. As with the investigation of the VOTs, the climber's verbalization was transmitted over the radio to the experimenter at the base camp and recorded.

The duration required to process sentences was influenced directly by degree of both high altitude and sentence complexity.<sup>79,80</sup> Interestingly, VOT separation width (in milliseconds) and the latency to process sentences were correlated  $-0.77$ .<sup>79,80</sup> This

correlation coefficient implies that 60% of the impaired processing of sentences under these conditions was predicted by the VOT index. Fortunately, these changes in speech and in processing of language were transient; they recovered after descent to the base camp (5,300 m).

This methodology, which is based on changes in speech, may be useful in other stressful situations that involve hypoxia, such as flying in aircraft (without cabin pressurization or supplemental oxygen); high-altitude parachuting; and aspects of mountain climbing. Because speech (real-time or recorded) is the basic datum for this technique, this methodology can be employed unobtrusively, at a distance, and (perhaps eventually) with automated equipment to aid analysis.

### **Sleep**

Mountain climbers, soldiers, hikers, tourists, and workers at high altitude have reported disturbed and fitful sleep.<sup>1,3,14</sup> People are seldom rested or refreshed even after a full night's sleep at HTE; respiratory periodicity with apnea (eg, actual pauses in breathing for 5–10 s during sleep) and sleep disruption occur.<sup>28,81–84</sup> Self-ratings of sleepiness increased after acute ascent to 1,600 to 4,700 m<sup>26,29</sup> or gradual ascent to 7,000 to 7,600 m.<sup>85</sup>

Scientific studies of sleep have been conducted under conditions of high altitude since the 1970s. Many studies were conducted in laboratory hypobaric chambers; others were conducted in tents or shelters at high altitude. In 1972, sleep was studied at high altitude for the first time with electroencephalography (EEG).<sup>86</sup> The investigation, carried out at 4,300 m at the US Army Pikes Peak Laboratory Facility, a part of the US Army Research Institute of Environmental Medicine (USARIEM), Natick, Massachusetts, found that sleep stages 3 and 4 decreased and periodic breathing occurred; however, total time asleep did not change. During days 1 through 12 at 4,300 m, EEG characteristics, the number of awakenings during sleep, and subjective ratings of sleep quality returned to sea-level values. In other investigations during acclimatization, changes in ventilatory and blood-gas measures were described for various sleep stages and wakefulness.<sup>84</sup> At higher altitudes (eg, 5,000 m), disturbances of sleep may last for many days or weeks.<sup>28</sup>

In 1975, Reite and colleagues<sup>86</sup> noted a disparity between objective and subjective measures of sleep quality at high altitude. These investigators suggested that the difference was related to the frequency of arousals during sleep and concluded that

the subjects' intense complaints were disproportionate for the situation. Reite and colleagues did not recognize that such brief arousals might disrupt sleep and dramatically influence subjective appraisals of sleep quality.

In 1985, EEG was used to study brain wave characteristics during sleeping, walking, and climbing in 12 males on an expedition to Mount Api (7,130 m) in the Himalayas.<sup>87</sup> This was the first study of sleep at high altitude that also included ambulatory EEG with free-roving climbers. Each climber wore a small portable medical (physiological) recorder to record EEG signals. Recordings were made during acclimatization from 4,115 m to 6,220 m. Collection of these data was a remarkable scientific and technological feat, especially under such challenging and extreme environmental conditions. Stage 4 sleep was reduced 65% to 74% at 4,115 m (compared with values at sea level); stage 4 did not change with altitudes higher than 4,115 m. Rapid eye movement sleep was also reduced at high altitude. During sleep, EEG records showed no gross abnormalities or epilepsy-like phenomena, nor did records during ambulation and climbing. These investigators were reassured that such abnormalities were not observed, because it was suspected (in 1985) that extreme altitude conditions might cause prolonged damage to the CNS in some climbers; the investigators thought that their climbers may have been "protected" by being well-acclimatized and by practicing good hydration discipline. However, this study provided evidence that sleep quality at high altitude was impaired even in well-maintained, healthy, and acclimatized climbers.

In 1985, during Operation Everest II, the male volunteers frequently reported that they slept poorly at night at high altitude. Their complaints included difficulties in falling asleep, frequent nighttime awakenings, and feeling less refreshed than expected on awakening. In 1992, Anholm and colleagues<sup>81</sup> modified procedures to score sleep EEG records and noted episodes of marked hypoxemia at night and several 3- to 4-second arousals during sleep (eg, they measured 22, 63, and 161 arousals per hour at 180, 4,572, and 7,620 m, respectively). Earlier efforts of these investigators established that traditional scoring of EEG records would not detect brief arousals of 3 to 4 seconds observed during sleep at high altitude, because brief arousals are not predominant phenomena in a 20- to 30-second scoring epoch.<sup>88</sup> Brief arousals were not observed in all apnea cycles; however, all volunteers experienced them.<sup>81</sup> These objective sleep data suggested many reasons for the complaints of poor sleep at high al-

titude. Compared with sea level, volunteers at 7,620 m experienced more frequent awakenings (37.2 vs 14.8), total sleep time was reduced (167 vs 337 min), rapid eye movement sleep was a smaller portion of total sleep time (4.0% vs 17.9%), and, as noted, brief arousals during sleep were more frequent.<sup>81</sup>

Looking closely at brief events in the EEG records from high altitude (ie, 4,572, 6,100, and 7,200 m), these researchers<sup>81,88</sup> found a relationship between the number of arousals during nighttime sleep and deficits in daytime performance. The number of arousals and the degree of apnea-induced hypoxemia during sleep were better predictors of daytime cognitive impairments than alterations in sleep stages. During nighttime sleep at altitude ( $\geq 4572$  m), values for arterial oxygen tension ( $P_{aO_2}$ ) were lower than those observed in the daytime<sup>28,81,84,88</sup>; such acutely decreased  $P_{aO_2}$  values in the daytime while awake would probably be lethal in an unacclimatized volunteer.<sup>28,81</sup> Sleep efficiency and number of awakenings during sleep did not change at altitudes higher than 4,572 m; higher than 6,100 m, however, volunteers were less active behaviorally and spent more time napping.<sup>81</sup> Rapid eye movement sleep was decreased by 70% during hypoxemia, but slow-wave sleep did not change.<sup>81</sup>

At 6,100 m, different sleep stages had minimal effects on the oxygen saturation of arterial blood ( $S_{aO_2}$ ); however,  $S_{aO_2}$  was negatively correlated ( $-0.72$ ) with the number of brief arousals during sleep.<sup>81</sup> The lowest values of  $S_{aO_2}$  in all five volunteers during the study were measured during sleep. The difference between daytime and nighttime  $S_{aO_2}$  values increased as altitude increased. All volunteers exhibited periodic breathing with apnea during much of the night at 6,100 and 7,620 m. Periodic breathing in all volunteers was central in origin, not obstructive. These data suggest that the use of supplemental oxygen during the evening (the equivalent of sleeping at a lower altitude) may improve sleep and, therefore, subsequent daytime performance.

Climbers and other team members often experience poor-quality sleep at high altitude and are tempted to take different medications to improve sleep.<sup>14,89</sup> Acetazolamide appears to be the best sleep-enhancing drug at high altitude because it reduces periodic breathing, improves oxygenation, and is a safe medication to improve sleep.<sup>89</sup> Sleep quality, quantity, and self-ratings of sleep characteristics are improved by the use of acetazolamide.<sup>82,83</sup> Other sleep-improving drugs at high altitude, such as diphenhydramine, triazolam, or temazepam, can be used; however, they are potentially dangerous because they depress

ventilation, relax the muscles of respiration, and further complicate conditions associated with hypoxemia at high altitude.<sup>82,83,89,90</sup> Therefore, the choice of an inappropriate sleep aid may increase hypoxemia, complicate sleep apnea at high altitude, and impair daytime cognitive performance in some individuals at high altitude. (Strategies for improving sleep at HTE and decreasing the adverse effects of exposure to altitude are also reviewed in Chapter 24, Acute Mountain Sickness and High-Altitude Cerebral Edema, and Chapter 25, High-Altitude Pulmonary Edema.)

A review by Heath and Williams<sup>28</sup> in 1989 examined the phenomena of nocturnal periodic breathing at high altitudes. Paradoxically, people with the greatest ventilatory drive in response to hypoxia in the daytime (an adaptive response) have the most pronounced periodic breathing at night.<sup>28,84</sup> The greatest effect of periodic breathing during sleep is that  $S_{aO_2}$  is reduced during sleep to less than what one would expect for that level of altitude during the daytime. This significant reduction during the nighttime affects both sleep quality and subsequent cognitive capabilities during waking hours. Several investigators reported that people at altitude whose arterial blood became the most desaturated at night also performed more poorly on daytime tests of cognitive performance.<sup>81,91</sup> Hence, subjects best able to adapt to hypoxemia and perform physical work during waking hours were most impaired in their daytime cognitive performances because of their ventilatory responses during sleep. This finding is also consistent with an experimental study<sup>92</sup> of sleep apneics at sea level that demonstrated that sleep apneics also experience daytime cognitive performance decrements resulting from their hypoxemia during sleep.

Currently, there is controversy as to whether daytime performance impairments in individuals with sleep apnea (at sea level) result from severe hypoxic episodes induced by apnea during sleep or from disrupted EEG sleep stages and associated fragmented sleep.<sup>93</sup> In a correlational study of patients with sleep apnea, the best predictor of the hypoxic aspects of apnea episodes was the number of episodes during sleep when  $S_{aO_2}$  fell by 4% or more.<sup>46</sup> This criterion of hypoxemia correlated with several of the patients' daytime performance measures but did not predict changes in sleep stages. Also, in the experimental study of patients with sleep apnea, daytime cognitive impairments were found to result from hypoxemic episodes during the evening and to a lesser extent from sleep fragmentation.<sup>92</sup>

Thus, in patients with sleep apnea, the degree of hypoxemia during sleep, rather than changes in sleep architecture, is correlated with impairments in daytime performance.

### **Neuronal Cells**

Severe, chronic hypoxia can produce permanent damage to neurons, depending on the severity of the exposure.<sup>94</sup> Evidence gathered from magnetic resonance imaging (MRI) during the 1990s supports the idea that some hypoxic CNS damage induced by HTE may be long-term.<sup>18,95</sup> Calcium appears to play an integral role in the production of ischemic and hypoxic cell damage. Ischemic damage to the plasma membrane of the cell disrupts its relative impermeability to calcium and results in an influx of calcium. Large accumulations of free calcium disrupt metabolic function and eventually cause neuronal death.<sup>96</sup> This massive increase in intracellular free calcium occurs preferentially in the cells that appear to be selectively vulnerable to ischemia.<sup>97,98</sup> Neuronal injury from hypoxia can be prevented if calcium accumulation is blocked.<sup>99</sup>

Histological studies with small laboratory animals showed that some cortical layers (III, V, and VI) and the hippocampus, striatum, thalamus, and amygdala are especially vulnerable to hypoxic damage.<sup>94</sup> Pyramidal cells in the hippocampus are vulnerable to ischemically induced damage; morphological degeneration of these cells occurs 2 to 4 days after the ischemic insult.<sup>98,100</sup> Severe ischemia (10–15 min in duration) extended neuronal death to other regions, such as the hippocampal CA3 and CA4 subfield, cerebral cortex, striatum, and thalamus.<sup>101</sup> Additionally, there is evidence that transient hypoxia (4.5% oxygen for 30 min) can induce irreversible neuronal damage in the CA1 subfield; such hippocampal lesions can result in deterioration of cognitive memory function.<sup>102</sup>

Repeated exposures to extreme altitude can cause mild but persistent cognitive impairment because the brain areas most vulnerable to chronic hypoxia seem to be the hippocampal structures.<sup>103</sup> The hippocampus, an area thought to be involved in learning and memory processes, is rich in cholinergic innervation; as shown by studies with rats, the central cholinergic system is particularly vulnerable to hypoxia.<sup>104</sup> Rats subjected to forebrain ischemia developed severe damage to the CA1 region of the hippocampus, which led to impaired behavioral performance on memory tasks.<sup>105</sup> Other investigators suggested that cognitive deficits correlated

more with cell losses observed in the CA2 and CA3 sectors than with damage to the CA1 region of the hippocampus.<sup>106</sup>

In yet another study with rats, morphological changes were observed with light microscopy in rats' brains following a 4-day exposure to altitude.<sup>77</sup> Damage was observed in some rats exposed to altitudes of 5,500 or 6,400 m, with cell degeneration and death increasing as altitude increased. Also, the longer the time following exposure before sacrifice, the more noticeable the damage, which suggests delayed neurotoxicity. These data suggest how exposure to extreme high altitude may result in permanent brain damage, but the conditions that cause such damage and the consequences of such damage on subsequent behavioral performance are only beginning to be determined.

### **Neurochemical Mechanisms**

The central mechanisms responsible for the effects of hypoxia on behavior and cognitive processes are not known. Additionally, none of the drugs currently employed to treat the effects of hypoxia, such as acetazolamide or dexamethasone, have specific mechanisms of action that act centrally.<sup>107</sup> Numerous studies<sup>69,104,108–111</sup> have sought to determine the effects of hypoxia on central neurotransmitters and their metabolites. The direct effects of mild transient hypoxia on the brain are likely to be variations in the level of specific neurotransmitters, transient morphological changes, or both. Because the synthesis of several neurotransmitters is oxygen-dependent, abnormalities of neurotransmitter metabolism may mediate the early functional changes due to acute hypoxia.<sup>104</sup> Some of the behavioral decrements caused by hypoxia may be attributable to changes in neurotransmitter utilization and concentration.<sup>108</sup>

The central cholinergic system is particularly vulnerable to hypoxia, and it appears that acetylcholine (ACh), which is involved in the regulation of learning and memory processes,<sup>108</sup> is the neurotransmitter primarily affected.<sup>104</sup> The rates of synthesis of other neurotransmitters (eg, dopamine, serotonin, and the amino acids), are also sensitive to hypoxia, but perhaps less so than the rate of ACh synthesis.<sup>109</sup> A decrease in ACh synthesis has been documented following mild hypoxia without any reduction in neuronal ACh concentration; this is consistent with the hypothesis that hypoxia acts through inhibition of ACh release.<sup>107,110</sup> Hypobaric hypoxia (equivalent to 5,500 m simulated altitude) reduced extracellu-

lar hippocampal ACh release,<sup>111</sup> lending support to the hypothesis that decreases in ACh metabolism and release are caused by altitude exposure. Impaired ACh synthesis and release could account for many of the behavioral symptoms of hypoxia.<sup>104</sup>

### Changes in the P300 Waveform

The P300 waveform, a positive, endogenous, event-related brain potential, provides a new tool for investigating cognitive performance impairments. This measure reflects the processes of evaluation rather than those involved with selecting or executing a response. Decreasing the  $P_{aO_2}$  increased P300 latencies and reaction times in an experimental study; hypoxemia had no effect on P300 amplitudes.<sup>112</sup> Measures of P300 latencies and reaction times to the stimuli were highly correlated, whereas P300 amplitudes and reaction times were not. Increased P300 latencies are thought to indicate that hypoxemia slows stimulus evaluation processes. Another study<sup>113</sup> demonstrated that both the reaction time and movement components of a reaction time task were affected by hypoxemia.

In 1993, Kida and Imai<sup>114</sup> investigated 38 male volunteers at successive levels of simulated altitude in a hypobaric chamber (0 m; 3,000 m; 4,000 m; 5,000 m; 6,000 m; and 0 m) with an auditory oddball reaction time paradigm. All altitude conditions were tested the same day; testing was for 45 minutes at each altitude. The volunteers were classified into three groups based on their auditory reaction times

for the different altitudes. This post-hoc classification yielded a group with increased reaction times at altitudes of 4,000 m; a second group with increased reaction times at 5,000 m; and a third group with no increases, not even at 6,000 m. Using this classification of responses to altitude, these investigators believed that they found several distinctive waveforms in event-related potentials that may be predictive of whether a person's cognitive performance will be vulnerable to hypoxia.

In 1995, Fowler and Prlic<sup>75</sup> investigated 6 volunteers to determine the influence of stimulus modality (vision or audition) on the slowing of the P300 waveform produced by hypoxia. Thresholds were estimated from measures of reaction time and the event-related brain potential P300. Volunteers responded to oddball light flashes or tone pips while breathing low-oxygen mixtures manipulated to produce  $SA_{O_2}$  of 77% to 86%. Both reaction time and P300 slowed in a dose-dependent manner with hypoxia, suggesting that the role of the stimulus-evaluation processes may be important in slowing. The threshold altitude for slowing was similar for both modalities (ie, 81%–82%  $SA_{O_2}$ ). The P300 amplitude exhibited an inverted-U dose-response function and was different from the response time measures. These investigators inferred that the slowing of reaction times and the P300 duration result from perceptual, rather than central, processes and that the inverted-U function for increasing hypoxia and P300 amplitude may reflect the activity of physiological compensatory mechanisms.

## VARIABLES THAT INFLUENCE EFFECTS AT HIGH TERRESTRIAL ELEVATION

A number of other variables besides the level of HTE contribute to the type and magnitude of the adverse psychological impairments observed after exposure to altitude. Some adverse effects are more sensitive to high altitude (eg, visual changes result at lower levels of HTE than the symptoms of AMS). The time courses of various adverse effects are often dissimilar; effects may begin, be maximal, or end at different times. The late 1980s also brought the recognition that very extreme altitudes may cause long-term, if not permanent, impairments in some cognitive and psychomotor performances. Characteristics of military, survival, or psychological assessment tasks, such as task complexity and the amount and distribution of practice on them, also influence adverse effects. Likewise, some characteristics of the soldier or the climber are also important. They include his or her strategy for optimizing speed versus accuracy of his or her performance on

a task, sensitivity to hypoxia, and individual differences that affect adverse psychological effects.

### Threshold Altitude for Effects

Knowing and predicting the effects of varying degrees of high altitude are of critical importance for many military and civilian enterprises and activities. This section is concerned with the altitude (threshold) at which illness and other adverse effects occur.<sup>3,115</sup> In planning for military operations at high altitude, commanders must consider how much illness and impaired performance must be anticipated at a given altitude.<sup>4,6,7</sup> Likewise, other personnel specialists also make similar judgments (eg, astronomers determine if supplemental oxygen is required in their observatories above 3,800 m<sup>14,15</sup>; and regulatory specialists in commercial aviation specify minimum altitudes [eg, 1,800–2,438 m] above which supplemental oxygen

or pressurization in the aircraft is required) based on high-altitude research and experience. Such guidelines are reevaluated periodically to ensure that human capabilities are sustained in especially demanding environments and that safety guidelines produce specifications that are not excessive (structural specifications, weight, and safety systems of aircraft or requirements for observatories).<sup>10</sup> Individual responses to high altitude, supplemental oxygen, or pressurization of an aircraft will vary greatly; other factors such as physical activity, smoking, heart and lung disease, and alcohol consumption will degrade a person's adaptation to a given level of altitude.<sup>10,15</sup>

Sensation, symptoms, moods, and physiological functions are more sensitive to the effects of high altitude than is cognitive performance.<sup>11</sup> Changes in cognitive functioning are usually reported for altitudes in excess of 3,048 m, whereas changes in sensation, symptoms, moods, and physiological functioning are often observed at lower altitudes. McFarland<sup>11</sup> reported the incidence for varied complaints in 200 volunteers at 3,048 m altitude as headache (10%), altered respiration (> 15% after 10 min), dizziness during locomotion (~ 4%), and sensory impairments (~ 5%). Thresholds for the dark-adaptation function were increased at 1,524 and 2,255 m; such increases were evident 2 minutes after the start of dark adaptation at 2,255 m.<sup>11</sup> Shukitt and Banderet<sup>29</sup> found increased sleepiness in volunteers at 1,600 m. Fraser and colleagues<sup>116</sup> reported increased postural sway at 1,521, 2,438, and 3,048 m; however, their statistical analyses and interpretations were challenged.<sup>117</sup>

Other variables than the degree of high altitude influence the threshold for effects, such as the dependent measure of interest. For example, the duration until one loses consciousness after exposure to HTE, such as during special altitude training in a hypobaric chamber, does not change until higher than 5,000 m,<sup>118</sup> whereas many other dependent measures of effects such as mood states would change after exposure to 3,000 m or 4,000 m. Other critical variables are the duration of exposure before measurements are assessed, the rate of ascent, the choice of dependent measures within a class of phenomena (eg, mood state of sleepiness vs dizziness),<sup>29</sup> and the statistical power of the study design.

Studies of psychological effects at altitudes of approximately 3,000 m or lower often have equivocal outcomes. Performance (rate of problem solving) on Baddeley's Grammatical Reasoning Test was not significantly impaired at 2,440 m or 3,050 m of altitude in four groups of 30 civilians<sup>119</sup>; interestingly, the authors of the study attributed the greater error rate at 3,050 m to apprehension rather than to the effects of

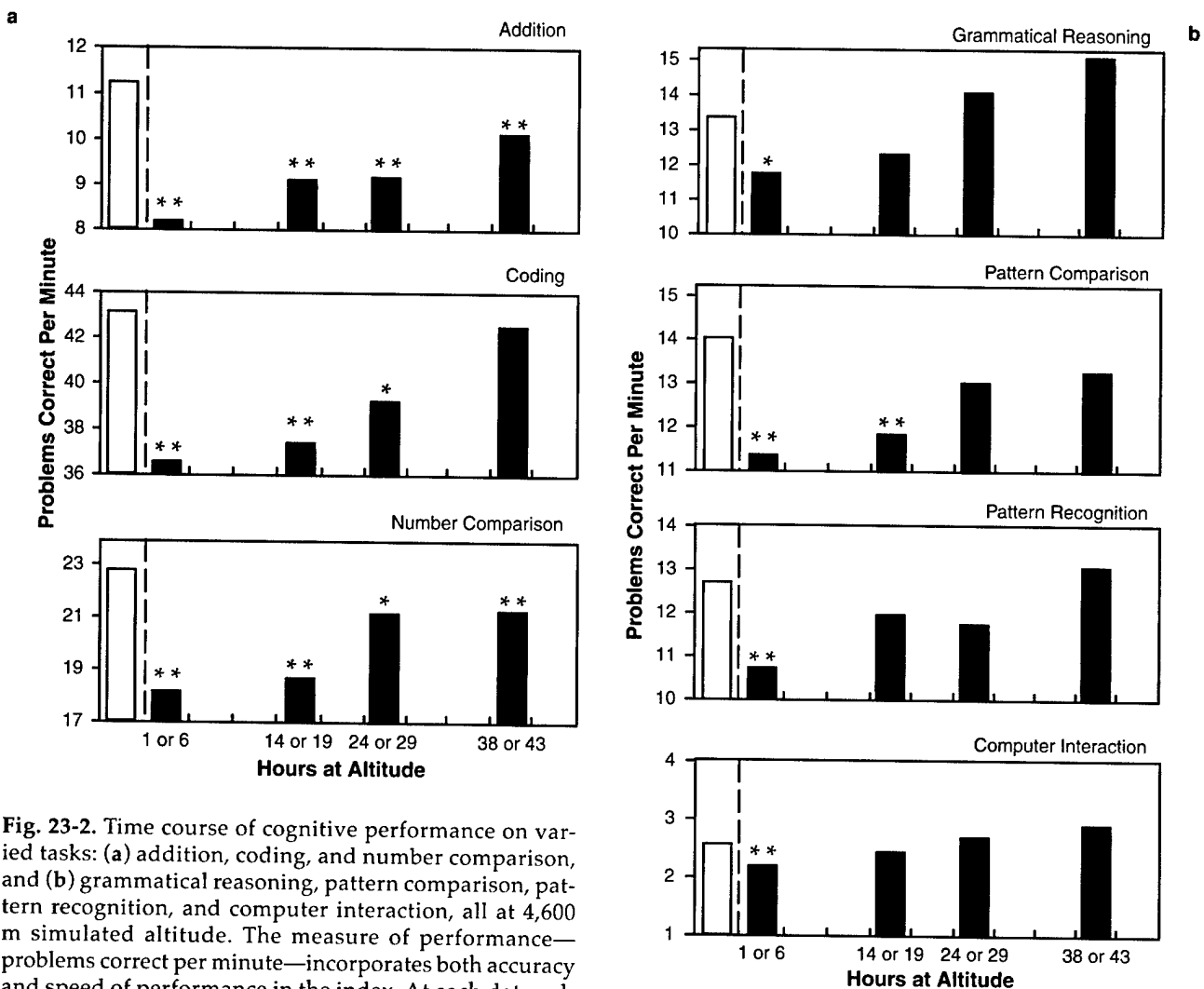
altitude per se. In a clinical study, seven subjects were exposed to 3,048 m for 6.5 hours.<sup>120</sup> When the effects of only responsive subjects were emphasized, subjects' cognitive performances appeared affected; inferential statistics were not used because of large individual differences.<sup>120</sup> At altitudes higher than 3,048 m, incremental changes were demonstrated with progressively higher altitudes for pattern perception, alertness, memory, computation, decision making, and attention.<sup>11</sup>

Tune's<sup>121</sup> 1964 literature review suggested that an altitude of 3,048 m or higher will cause perceptual-motor impairments. However in 1966, Denison, Ledwith, and Poulton<sup>122</sup> found increased reaction times on a spatial task while subjects exercised at 2,438 m, an altitude 650 m lower than that specified by Tune.<sup>121</sup> They suggested that task novelty, resulting from new learning of task information, made performance more vulnerable at these low altitudes. Guided by these data, the recommendation was made that cabin altitudes in aircraft (cabin pressures) be maintained below the equivalent of 2,438 m to ensure the performance of aircrews.<sup>9</sup> A more-recent investigation (1995) evaluated 12 male volunteers at simulated altitudes of 30 m, 2,134 m, and 3,658 m with a signal-detection approach and found that response times were slower at the two high altitudes.<sup>123</sup> These investigators suggested 2,134 m as a threshold for effects in this study—an unexpectedly low threshold value. Another explanation for this lower threshold is that it is an artifact, since the variability of  $\text{Sao}_2$  from person to person can be great (eg, 82%–98%, with a mean of 91.2%) when ambient pressure is manipulated to simulate a specific altitude condition. Hence, the variability of  $\text{Sao}_2$  values (which can result from manipulating ambient pressure) or the greater sensitivity of the signal-detection paradigm that was used may account for these apparent effects at 2,134 m.

Many performances appear more robust to the effects of hypoxemia than was suggested by the two investigations just described.<sup>122,123</sup> In 1963, Tichauer<sup>124</sup> studied machine shop operators producing bicycle axles at 2,740 m and observed that their performance at that altitude was not different from sea-level performance; such tasks were affected in shops at 4,120 m. It is likely that some of the conflicting work on the minimum threshold for altitude effects may depend on whether the researcher controlled  $\text{Sao}_2$  or ambient pressure. In 1985, Fowler and colleagues<sup>125</sup> attempted to replicate the 1966 study of Denison and colleagues,<sup>122</sup> and found that altitudes higher than 2,134 to 2,438 m were required to produce the effects that had been suggested by Denison and colleagues. The Fowler investigation also showed the importance of

controlling  $P_{aO_2}$  (a measure highly correlated with  $SA_{O_2}$ ), rather than atmospheric pressure or gas mixtures, to ensure comparable hypoxemia. They concluded that the findings of Denison and colleagues<sup>122</sup> probably resulted from unusually low arterial  $P_{aO_2}$ , caused by the resistance of breathing through a facial mask, which became more significant during hypoxia, exercise, and hypoventilation. Hence, Fowler and colleagues<sup>125</sup> concluded that 2,438 m was substantially lower than the actual altitude threshold that affects performance. Their investigation also suggested that new learning is no more vulnerable than prior learning to the effects of hypoxemia.

To determine the minimum altitude that causes changes on perceptual motor performance, in 1987 Fowler and colleagues<sup>126</sup> established altitude-response curves for the serial choice reaction time task for two levels of stimulus brightness.  $P_{aO_2}$  was manipulated in small increments by having six subjects breathe low-oxygen gas mixtures so that varied levels of hypoxemia (simulating altitudes of 2,712–3,475 m) were produced. Response times slowed in an altitude-dependent manner; the minimum altitude (ie, the threshold) for effects was estimated at 2,972 m. These data from a choice reaction time task are strong support for Tune's assertion in 1964 that the minimum



**Fig. 23-2.** Time course of cognitive performance on varied tasks: (a) addition, coding, and number comparison, and (b) grammatical reasoning, pattern comparison, pattern recognition, and computer interaction, all at 4,600 m simulated altitude. The measure of performance—problems correct per minute—incorporates both accuracy and speed of performance in the index. At each data collection interval, some of the volunteers were evaluated at one time and the remainder at a different time (eg, 1 h or 6 h). Asterisks above a bar indicate a statistically significant difference ( $P \leq .05 = *$ ;  $P \leq .01 = **$ ) from the baseline (200 m) value. Data source: Banderet LE, Shukitt B, Crohn EA, Burse RL, Roberts DE, Cymerman A. Effects of various environmental stressors on cognitive performance. *Proceedings of the 28th Annual Meeting of the Military Testing Association*. Mystic, Conn: US Coast Guard Academy; 1986: 594. DTIC No. AD 188762.

threshold for altitude effects on most performance tasks is approximately 3,050 m.<sup>121</sup> Hence, an earlier estimate of the minimum altitude that produces performance impairments (ie, 2,438 m), and its implied requirements for greater aircraft pressurization, was unnecessarily cautious.<sup>125,126</sup>

### Time Course of Effects

Because adverse changes in mood and cognitive performance occur after exposure to high altitude, two interesting questions are "What is the time course of these effects?" and "Are adverse changes in mood and cognitive performances related to increases in AMS?" The number, severity, rapidity of onset, and the duration of symptom, mood, and performance changes vary from person to person and are related to both level of altitude and rate of ascent.<sup>42,44</sup> The faster one ascends and the higher one climbs, the more likely the chances of being affected.<sup>3,42</sup> It is usually assumed that individuals afflicted with AMS will be more susceptible to changes in mood, cognitive and psychomotor performance, and the like; however, their time courses are sometimes different and may reflect different mechanisms.<sup>42</sup>

Symptoms of AMS start to appear after 6 hours, increase from 6 to 24 hours, and reach maximum severity during 30 to 40 hours of exposure.<sup>3,127,128</sup> The time courses of other factors measured by the Environmental Symptoms Questionnaire<sup>32-35</sup> (eg, cold, alert, exertion, muscular discomfort, fatigue) and some mood states appear similar to that of the symptomatology of AMS (AMS-C, the "cerebral" factor on the Environmental Symptoms Questionnaire), although these trends are not as well documented.<sup>29,44</sup> At 4,300 m, moods (friendliness, clear thinking, dizziness, sleepiness, and happiness) were adversely affected after 1 to 4 hours on the day of arrival and differed most after 18 to 28 hours.<sup>29</sup> By 42 to 52 hours after ascent, all moods returned to baseline levels. Adverse changes in mood states were also measured 90 minutes after ascent to a 4.5-hour exposure to 4,200 or 4,700 m during the first administration of the cognitive tests and mood questionnaires.<sup>30,129</sup>

The time course of performance impairments, however, appears somewhat different than that for AMS and some moods. Decrements on all seven tasks administered 1 or 6 hours after ascent to 4,600 m have been found.<sup>43,45,130</sup> At 14 hours or 19 hours, only four tasks were still impaired, and by 38 hours or 42 hours, only two were still impaired (Figure 23-2). Therefore, changes in performance were greatest at 1 hour or 6 hours (ie, soon after ascent), a time when the symptoms of AMS are only starting

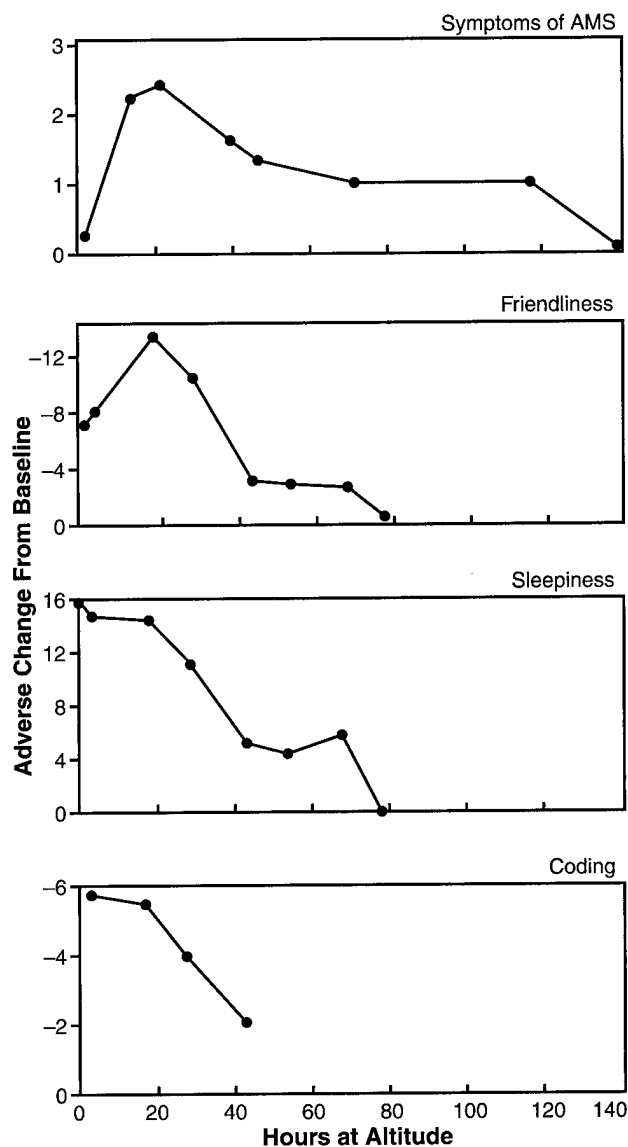


Fig. 23-3. Adverse changes at 4,300 m simulated altitude for selected measures of symptoms of acute mountain sickness (AMS), moods, and cognitive performance. The units for each dependent measure were retained but transformed so that baseline for each measure equals 0. The first three measures (symptoms of AMS, friendliness, and sleepiness) are based on subjective ratings; the fourth, coding, is a measure of cognitive performance and is scored as the number of problems correct per minute. Symptoms of AMS and the mood state friendliness have similar time courses. The time courses of sleepiness and coding are analogous but different from those for AMS and sleepiness. The time courses of coding performance and the symptoms of AMS, however, are dissociated and dissimilar.

to appear. Figure 23-3 emphasizes the dissociation between performance impairments while doing coding, the cognitive task, and the symptoms of AMS; performance on the coding task was some-



what improved when the symptoms of AMS were most severe (after 20–30 h). It also shows that the mood state of friendliness had a time course like that of AMS, whereas sleepiness had a time course like that of coding performance.

A study by Cahoon<sup>131</sup> in 1972 exposed volunteers to 4,570 m for 48 hours, during which they performed four card-sorting tasks after 3 hours, 20 hours, 24 hours, and 45 hours of exposure. The greatest decrement on all tasks occurred during the test at 3 hours; after that, performance improved. Other studies<sup>16,30,43,129</sup> have confirmed that adverse changes in cognitive performance were measured at 90 minutes of exposure to 4,200 or 4,700 m simulated altitude, which was the earliest that performance tasks were administered at altitude.<sup>30</sup>

### **Temporary Versus Long-Term Effects**

There is growing concern, heightened dramatically in the past 10 years, that some undesirable consequences of extreme high-altitude exposure may be long-term or even permanent. Mountain climbers, balloonists, and pilots who did not use supplemental oxygen have known that high altitude produces changes in affective behavior, judgment, and cognitive performance.<sup>1,2</sup> Long-term residents at even moderate altitudes of 4,328 m had 3- to 4-fold more migraine headaches than residents at sea level; tension headaches, however, were not affected.<sup>132</sup> Peter Habeler—who climbed Mount Everest in 1978 with the mountaineer Reinhold Messner, together making the first ascent without supplemental oxygen—suffered nightmares and memory lapses even a few years after the climb.<sup>72</sup> A case study described the fate of a man who was briefly subjected to 7,620 m during a malfunction in a hypobaric chamber.<sup>133</sup> Although the man was revived and quickly returned to sea level, 15 years later he still experiences loss of taste and throbbing headaches in both temples three or four times weekly. Some medical professionals (some of whom are also climbers) express concerns that extreme climbs (almost resulting in death or completed without supplemental oxygen) may produce long-term behavioral and cognitive changes.<sup>18,134</sup>

Practices that put climbers at unnecessary risk for CNS damage also raise another concern: some neurological effects of extreme exposures to high altitude may be latent and have minimal impact until the brain is subsequently traumatized by another injury or stressor.<sup>135</sup> If so, an earlier impairment from climbing could combine with and magnify the degradation from a new trauma.

In a review prepared in 1989, Banderet and Burse<sup>42</sup> concluded that long-term effects caused by ascent to extreme high altitude were a reliable and important phenomenon. At that time, there were many older studies with no adverse findings; only a few new studies supported the idea of extreme high altitude causing long-term effects to the CNS. In that review, they said:

New trends in climbing increase the risk of damage to the nervous system, since some climbers choose special procedures to deliberately increase the challenge of climbing high mountains.<sup>[40,134,136]</sup> Climbers may ascend without time scheduled for staging, without supplemental oxygen, during the winter, or without securing ropes.<sup>42(p240)</sup>

Since then, it has become clear that many factors are putting greater numbers of climbers at risk for long-term, perhaps permanent, CNS effects. Climbing without supplemental oxygen has become fashionable in the last few years, since a small group of elite climbers has scaled all 14 of the peaks above 8,000 m in the world without supplemental oxygen.<sup>18</sup> (Some mountain climbers, from Russia, for example, choose not to use supplemental oxygen during a climb because they feel it is unethical and wrong to use it.<sup>137</sup>) In addition, blatant commercialism and promotion of climbing expeditions to extremely high altitudes expose inexperienced and unseasoned climbers to perilous conditions.

What data support the idea that climbs to very high altitudes engender long-term changes to the CNS? Studies demonstrating such effects were rare before and during the 1980s. More than 100 climbers who spent time above 5,500 m in the mid 1970s indicated by survey that they did not feel that they or their peers were permanently impaired by altitude.<sup>1</sup> More than 20 individuals who climbed higher than 5,300 m were carefully studied by means of several psychological tests; these data, published in 1983, supported the earlier findings of no long-term effects.<sup>138</sup> Climbers who spent at least 4 days above 7,200 m, and two who reached the summit of Mount Everest, were assessed in 1989.<sup>139</sup> Temporary impairments were observed during the climb at altitudes higher than 5,200 m; after descent, there was no evidence of impairment.

Recent studies provide much stronger evidence for long-term effects by documenting both behavioral and structural phenomena. Personality and mental effects were documented in 80 Polish Alpinists from 1960 through 1985. In some climbers, permanent injury to the CNS was inferred because of

the persistence of mental changes long after the climb.<sup>40</sup> In 1985, Townes, Hornbein, and Schoene<sup>140</sup> studied 51 climbers from five expeditions to Mount Everest. Various neuropsychological tests suggested transient changes in verbal expression and possibly memory. Most remarkable and persistent was a bilateral motor impairment even 1 year after the climb. Such changes at high altitude and immediately after descent were replicated in Operation Everest II.<sup>91</sup>

Impairments after high-altitude exposure have also been demonstrated for HTE less extreme than Mount Everest. Long-term effects from climbing to 5,947 m were demonstrated in 1993.<sup>141</sup> Also in 1993, Kramer, Coyne, and Strayer<sup>48</sup> published their comparison of 18 men and 2 women who climbed Mount Denali (6,194 m) in Alaska with their matched controls. After descent, the climbers showed deficits of learning and retention in perceptual and memory tasks. With each administration of the memory search and choice reaction time tasks, the climbers responded more slowly on these tasks than the control group, demonstrated less transfer from practice on the tasks, and were more disrupted by the time intervals between practice sessions.<sup>48</sup>

Memory studies in seven people who climbed without supplemental oxygen to 7,100 m were published in 1987; even 75 days after the climb, memory impairments persisted.<sup>95</sup> A subsequent study with 10 climbers (9 men and 1 woman) who spent 14 days at 5,300 to 7,000 m without supplementary oxygen confirmed memory deficits even 75 days after the climb.<sup>142</sup> The investigators speculated in 1990 that the impairments were created by the effect of extreme hypoxia on the temporal lobes.<sup>142</sup> They were surprised to find the impairments in this study, as this climb was made during the summer so that atmospheric pressure and weather conditions would be less severe than during the other seasons. Still another study,<sup>141</sup> published in 1993 by this same team of investigators, studied 11 male climbers from two separate expeditions who ascended to 5,947 or 7,439 m without supplemental oxygen; all climbers spent at least 14 days above 5,200 m. Seventy-five days after the climbers returned to sea level, testing showed that measures of associative memory, reaction times, and concentration were impaired, compared with their performances before the climb. The investigators suggested that one climb may have been sufficient to produce these effects because (1) none of these climbers had climbed before outside the Alps and (2) none were professional climbers.<sup>141</sup>

In 1989, Regard and colleagues<sup>103</sup> measured small

impairments in concentration, short-term memory, and ability to shift concepts and control errors in five of the eight world-class climbers that they studied who had scaled mountains approximately 350 m lower than Mount Everest. Some 2 to 11 months earlier, all climbers had been at altitudes above 8,500 m for 2 to 15 days.<sup>103</sup> More-detailed analyses of these climbers' performances published the next year<sup>65</sup> indicated that although all climbers were highly motivated and achievement oriented, the performance of five of the eight climbers showed significant decrements of concentration, short-term memory, and cognitive flexibility. Their perceptual abilities, language, and spatial-constructive abilities were intact so the measured impairments in the five climbers affected probably reflected mild, but permanent, malfunctioning of fronto-temporo-basal brain areas. Conventional EEG recordings, evaluated by two independent experts, showed pathological findings in the two climbers with the greatest cognitive impairments. After their ascent, seven of the eight climbers underwent evaluation of their brains and spinal cords with MRI. The two climbers who showed abnormal MRI findings were among the most cognitively impaired.<sup>65</sup>

Hornbein and colleagues<sup>91,143</sup> tested 35 mountaineers before and 1 to 30 days after ascent to 5,488 and 8,848 m, and 6 volunteers before and after a 40-day ascent to a simulated altitude of 8,848 m. Impairments were manifested by deficits in memory phenomena (storage and recall), aphasia, concentration, and finger-tapping speed.<sup>143</sup> Visual long-term memory was impaired in both groups after descent; however, the mountaineers made twice as many aphasic errors after, compared with before, the climb.<sup>91</sup> Each person's cognitive impairment was positively correlated with his or her ventilatory response to hypoxia.<sup>91,143</sup> Verbal long-term memory was also affected, but only in the volunteers experiencing altitude in a hypobaric chamber.<sup>91</sup> This finding from the laboratory study is of special interest because it suggests that even when the hardships and extreme conditions (eg, cold and storms) associated with climbing a mountain are minimized, cognitive impairments may still persist several days after descent.

Further support for long-term effects was provided by a study<sup>144</sup> of 26 male and female climbers who did not use supplemental oxygen during ascents to extreme HTE. After descent from 7,000 m or higher (7,000–8,848 m), 46% of the climbers had abnormalities detected by MRI, and 58% had significant neurobehavioral impairments. The MRI images for the climbers and matched personnel

were scored blind by experts; no MRI abnormalities were observed in any of the 21 matched age and gender controls. The MRI abnormalities suggested cortical atrophy (19% of climbers) and hyperintensity lesions (19% of climbers); two climbers (8%) exhibited both of these MRI abnormalities. The MRI abnormalities that were observed were not associated with age, gender, clinical symptoms, maximal altitude climbed, or duration of exposure to HTE.

Some<sup>1,137</sup> believe that the physical trauma, dehydration, and weight loss at HTE (such as Ryn<sup>40</sup> and others) are responsible for such long-term changes. In contrast, others<sup>48</sup> suggest that the experimental design and assessment methodology are critical, or such effects may be missed. The latter emphasize that they would not have found such effects in their climbers without the use of matched controls. The study of Kramer, Coyne, and Strayer<sup>48</sup> also demonstrates that cognitive impairments after descent may result from a failure to profit fully from practice or the continued performance of a cognitive task. This insight may be a critical new dimension for evaluating the impact of such impairments induced by exposure to extreme HTE.

Others accept the data and conclude that such studies demonstrate long-term impairments. J. B. West, a researcher, physician, and climber, was the first to recognize such long-term effects (in 1986) and called early for an increased awareness of these phenomena, because unless they are informed, climbers, physicians, and educators cannot appraise the risks and choose conditions appropriate for long-term well-being.<sup>134</sup> In a review article<sup>18</sup> that also supports the idea that long-term effects are associated with extreme exposure to high altitude, these concerns were reinforced by the work of others. For example, Cavaletti and colleagues<sup>18</sup> are strongly convinced that climbing to extreme altitudes without supplemental oxygen may create long-term changes in the CNS that affect cognitive and memory processes. They assert that researchers, physicians, and climbers have an ethical responsibility to be aware of these data and to inform relevant others.

### Cognitive Task Complexity and Practice

Complex performances are usually affected before simpler performances,<sup>59,145</sup> so activities requiring decisions and strategies are more vulnerable than automatic processes.<sup>47</sup> Cognitive performance is more vulnerable to hypoxemia than is psychomotor performance.<sup>46</sup> Performances involving visual processing of shapes, patterns, and contours

are thought to be more vulnerable to impairments at altitude than those involving numbers, words, or characters.

The trends for complexity of the task were nicely illustrated by various displays of the Manikin Task. The effects of staging for 5 successive days at 4,500 m to 7,000 m were investigated (8 h/d) in an altitude chamber.<sup>146</sup> Measures of cognitive performance were determined from four male climbers with a mental rotation task (eg, a Manikin Task), during the acclimation procedure. The latency to mentally rotate simpler manikin displays was not affected by any altitude, not even 7,000 m (eg, rear view requires rotation about one axis only). At 6,500 and 7,000 m, responses to more complex displays of the manikin required longer latencies and climbers also made more errors than at lower altitudes. It is significant that these were experienced climbers; unacclimatized personnel probably would not have tolerated these altitudes.

Two vigilance tasks that varied in difficulty were investigated at a simulated altitude of either 610 or 2,438 m.<sup>147</sup> In this experiment, large numbers of volunteers were tested in both conditions of task complexity. The easier task was investigated with 44 volunteers; the more difficult, with 36. With the easier task, there was no significant difference between performance at either altitude. With the more difficult task, the volunteers' initial performance was significantly worse for the high-altitude group compared with the control group's. The impairment in performance observed initially at high altitude did not occur during the last half of the test trials.

The amount of practice on a cognitive task indirectly affects its sensitivity to the effects of high altitude. Thirty-six medical students performed a vigilance task at a simulated altitude of 2,438 m, and their performance was compared with that of a control group at 610 m.<sup>148</sup> If the students were not familiar with the test before assessment, the hypoxic participants performed poorer on the first half of the test than did the control group; there was no significant difference between groups on performance of the last half of the test. When the students become familiar with the test before exposure to high altitude, the performance of hypoxic and control participants was not statistically different.

In another study,<sup>62</sup> during a gradual mountain ascent (> 6,500 m) climbers served as data collectors by encoding responses and recording audio information for subsequent analysis. Reliability and validity checks of the data-collector climbers indicated that 36% of all errors happened during the first test session at 1,200 m. Overall accuracy for

the entire study was 99.6%. It is clear that additional practice and familiarization during the first data-collection session greatly improved subsequent performance, even when it was at high altitude.

### **Individual Differences**

Studies conducted at altitude frequently show large individual variations in dependent measures among volunteers; there appears to be wide individual response to the effects of altitude. Carson and colleagues,<sup>127</sup> describing the effects of 4,300 m high altitude, reported:

Variability in the degree of symptomatology of AMS is the rule rather than the exception. In our experience with placebo or untreated subjects on Pikes Peak, 10–20%, on the average, appear almost unaffected and 40–50% are temporarily incapacitated.<sup>127(p1085)</sup>

Others assert that the effects of altitude vary greatly from person to person, and some people show great variations from time to time. Such individual differences result from genetic, experimental, and psychological factors.<sup>14</sup>

Individual differences in response to altitude may explain why some studies have shown more pronounced effects of altitude than others. Barach<sup>25</sup> alluded to the difference in behavior that is produced by the environment in which the individual is tested for the effects of hypoxia. In a study with male volunteers, when the experimenter was an attractive female physician, the manifestations of impairment of emotional control differed greatly from those previously observed when the experimenter was a man. When a series of medical students and a group of patients were exposed to an atmosphere of 13% oxygen (simulating approximately 3,660 m altitude) for a 3-hour period, about 60% of the subjects registered euphoria, elation, and boisterous excitement, whereas 40% showed depression, mental dullness, and drowsiness from the start. In the male volunteers who manifested the euphoric tendency, exaggerated self-esteem and frank sexual advances toward the female experimenter were frequently encountered.<sup>25</sup>

The impairment in emotional control that is the result of hypoxia is also determined by the personality and behavior of the individual.<sup>25</sup> Mental efficiency and performance of discrete motor movements were affected at altitudes of 3,660 m,<sup>11</sup> and some individuals experienced altitude-related symptoms such as sleepiness, fatigue, and euphoria. Limited physical exertion at high altitude ap-

peared to minimize symptoms<sup>149</sup>; however, individuals with superb physical conditioning were just as likely to experience the effects of high altitude and the symptoms of AMS.<sup>150</sup> Athletes, however, generally tolerate discomfort well; although symptomatic, they may appear less affected by the illness than nonathletes.<sup>151</sup>

Some individuals believe that altitude will have a great effect on themselves, their performance, or both, while others believe that altitude will have little or no effect. Perhaps this could explain why some individuals' performance and moods are greatly affected at higher elevations, but not others'. Previous exposure to altitude may also influence an individual's psychological response to altitude. In other words, prior exposure might help to remove psychological barriers.<sup>151</sup> Additionally, motivation and training can effectively compensate for the stress imposed by a high-altitude atmosphere, with motivation a more important factor than training in maintaining performance at high altitude.<sup>49</sup>

In 1957, Greene<sup>152</sup> described several effects of chronic hypoxia. For example, chronic hypoxia affects people differently. It influences what system or process is affected and how greatly it is affected. Typically, memory is seriously affected, although the degree of impairment varies from person to person. The capacity to perform mental work accurately is usually degraded. Lastly, Green observed that an afflicted person's emotional instability may be severe, usually taking the form of irritability.

Sensitivity to hypoxia is an individual difference that affects one's responses to high altitude. Hypoxia normally causes an increase in breathing rate, breathing depth, or both; this increase is normally an adaptive response to hypoxia because it results in greater oxygen availability for delivery to the brain, tissues, and bodily organs. Surprisingly, researchers<sup>81,91</sup> found that climbers with the greatest sensitivity to hypoxia were the most hypoxic during sleep; these climbers also had some of the largest daytime cognitive performance deficits. Hornbein and colleagues<sup>91</sup> found that a greater ventilatory response to hypoxia correlated with a reduction in verbal learning and poor long-term verbal memory after ascent. A greater ventilatory response to hypoxia also correlated with an increase in the number of aphasic errors on the aphasic screening test in both the simulated-ascent group and a subgroup of 11 mountaineers. They concluded that persons with a more vigorous ventilatory response to hypoxia have more residual neurobehavioral impairment after returning to lower elevations. According to Hornbein and colleagues, this finding may

be explained by poorer oxygenation of the brain despite greater ventilation, perhaps because of a decrease in cerebral blood flow caused by hypocapnia that more than offsets the increase in arterial oxygen saturation.

Hornbein and colleagues<sup>90</sup> state that increased oxygen delivery to muscle during exercise is responsible for the finding that people with greater hypoxic ventilatory responses (who appear more impaired cognitively after exposure to extremely high altitude) are the ones who seem to perform best physically at great heights. On the other hand, Herr<sup>153</sup> suggests that the cognitive impairment demonstrated by Hornbein and colleagues<sup>91</sup> may be the link between a greater ventilatory response to hypoxia and better physical performance. The impairments may be associated with a mild decline in neurobehavioral function that blunts pain, leading to both better physical performance and the recollection of having performed better.<sup>153</sup>

### Performance Tradeoffs of Speed Versus Accuracy

Performance impairments at high altitude can reflect increased errors, slowing of performance, or a combination of these effects. Banderet and colleagues<sup>130</sup> studied cognitive tasks requiring processing of numbers, words, and patterns under conditions of cold, dehydration, and simulated altitude (4,300–7,600 m). Before the experiment, subjects practiced the tasks extensively, received performance feedback, and maintained low error rates. During exposure to each stressful environment, the rate of problem solving decreased; a few errors resulted but contributed little to the impairments. Such trends for varied high altitudes are shown in Figure 23-4.<sup>130</sup> Data were not collected for each altitude for all cognitive tasks. The average change in performance (from baseline) for the volunteers tested in each high altitude condition is shown for the contribution from increased errors or the contribution from decreased rates of performance. Although some errors occurred, it is clear that the strategy observed in these studies at varied high altitudes was a slowing of performance while maintaining accuracy. This strategy is consistent with that observed by us for other stressful, nonaltitude conditions.<sup>130</sup> These findings illustrate a common functional strategy observed in several studies where the volunteer sets the pace of the task: the rate of performance is often sacrificed for accuracy.<sup>46,145</sup> With time, performance at 4,600 m recovered to rates observed previously at low altitude; there was also a slight decrease in the number of

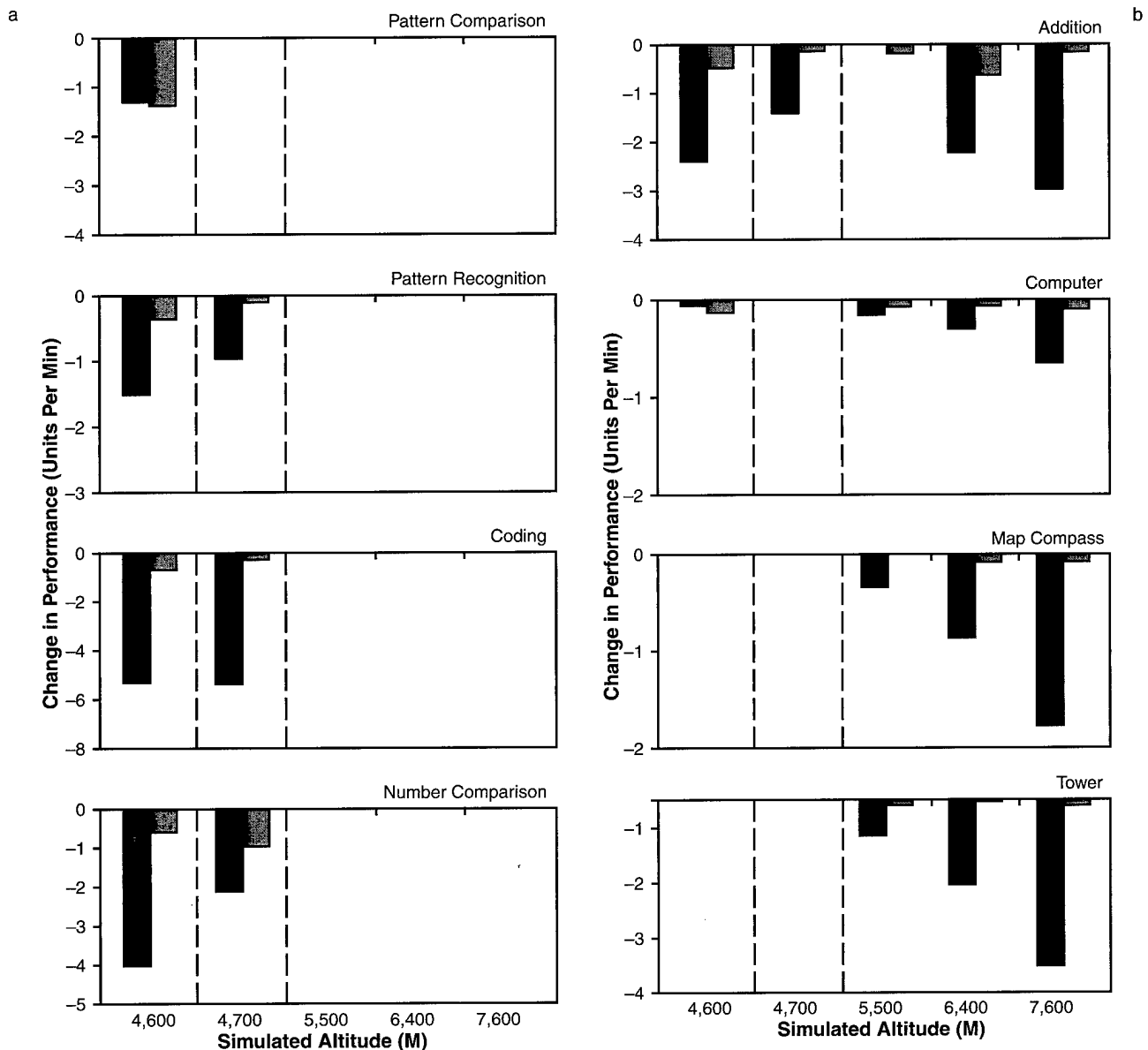
errors.<sup>43,130</sup> Other analyses suggested that the rate of each person's performance at low altitude (baseline) does not predict performance impairments resulting from altitude or other environmental stressors.<sup>43,130</sup>

Cahoon<sup>131</sup> studied eight participants with cognitive and psychomotor tasks at 4,570 m for 48 hours or less and found that cognitive tasks showed a greater decrement in speed and accuracy than simple tasks. Moreover, speed was generally sacrificed to maintain accuracy. Cognitive data, collected at altitudes from 5,500 to 7,600 m from six or seven volunteers in the Operation Everest II study, also exhibited a slowing of the rate of response for tasks administered by computer<sup>61</sup> and paper-and-pencil tasks.<sup>130</sup> Tapping keys on a computer keyboard with fingers on the preferred or nonpreferred hands was not affected.<sup>61</sup> These studies are consistent with the notion that hypoxemia affects cognitive functioning more than motor functioning.<sup>61,131</sup>

Investigators<sup>123</sup> used a signal detection approach to evaluate responses in 12 male volunteers to altitudes of 30 m, 2,134 m, and 3,658 m, simulated in an altitude chamber. On each trial, volunteers indicated if one of four symbols (rectangle, ellipse, the letter "A," or the numeral "1") was upright or rotated up to 90° counterclockwise by pressing one of two keys. Response times were slower at 2,134 m and 3,658 m than at 30 m. Also, a signal-detection analysis showed that at 2,134 m the accuracy of the volunteers' judgments about the orientation of the symbols decreased; their response criterion did not change.<sup>123</sup>

Twenty climbers from the Birmingham Medical Research Expeditionary Society were investigated during two separate climbs to 5,000 m. Climbers who were ill with AMS had increased reaction times. Increased errors also occurred, but they were not related to altitude or symptomatology.<sup>57</sup>

Tharion and colleagues<sup>60</sup> investigated the effects of acute and chronic hypoxia on marksmanship (days 2–4 and days 15–17 after ascent) resulting from residence at 3,700 to 4,300 m. Volunteers fired a laser-equipped training rifle at a 2.3-cm target 5 m away. Performance when firing a rifle during days 2 through 4 at high altitude was 9% less accurate than that at sea level, but the time taken for sighting was briefer at altitude. The change in performance strategy during acute exposure to altitude suggests a different speed–accuracy tradeoff or shift than that described previously: volunteers fired more quickly but less accurately at altitude than at sea level. During days 15 through 17 at high altitude, both measures of performance (timeliness and



**Fig. 23-4.** Contributions of increased errors (shaded bars) or slowing of performance (solid bars) to performance impairments observed at varied simulated high altitudes. These graphs show data for (a) the pattern comparison, pattern recognition, coding, and number comparison tasks at altitudes of 4,600 m and 4,700 m (except for the pattern comparison task, which was done only at 4,600 m), and (b) the addition, computer (computer interaction), map compass, and tower tasks (which, except for the addition task, were not collected for all altitudes). These data suggest that the performance impairments at high altitude on these cognitive tasks result primarily from a slowing of performance rather than decreased accuracy (ie, increased errors). Adapted with permission from Banderet LE, Shukitt B, Crohn EA, Burse RL, Roberts DE, Cymerman A. Characteristics of cognitive performance in stressful environments. *Proceedings of the 28th Annual Meeting of the Military Testing Association*. Mystic, Conn: US Coast Guard Academy; 1986: 427.

accuracy) were similar to those at sea level<sup>60</sup>; this suggests that after 15 to 17 days, performance at altitude had recovered to that observed earlier at sea level. Evans<sup>59</sup> studied eight men on a pistol-fir-

ing task at sea level and at 4,300 m. His results show a different speed-accuracy tradeoff than that of Tharion and colleagues<sup>60</sup> or the ones shown previously in Figure 23-4.<sup>130</sup> In Evans's<sup>59</sup> study at high

altitude, volunteers both took longer to fire and were less accurate at altitude than at sea level. These studies illustrate the importance of using measures that include both the speed and the accuracy of performance; otherwise, shifts or tradeoffs in performance criteria will not be evident and interpretations of the data may be misleading.

Schlaepfer, Bartsch, and Fisch<sup>67</sup> evaluated the effects of 3,450 m by transporting 10 volunteers to the Jungfrauoch (in the Swiss Bernese Alps) by helicopter, and by evaluating 10 other volunteers with gas mixtures equivalent to altitudes of either 3,450 m or sea level. All volunteers exposed to hypoxic conditions were assessed 15 minutes after exposure. The dependent variable involved systematically increasing the duration that letters were presented tachistoscopically each time a letter was identified incorrectly, until eight successive letters were recognized correctly. This study suggested that visual perception was improved by hypoxemia, because a briefer presentation was required for both the mountainous and the hypoxic gas-mixture conditions. Unfortunately, accuracies for the different conditions were not specified. Assessment 15 minutes after exposure may have changed the volunteers' response criteria (factors unrelated to the stimulus properties, eg, experience with the task) without any changes in stimulus discriminability occurring. Without more information, it cannot be determined if the reported trend reflected a shift in the volunteers' speed-accuracy tradeoffs.

Another study<sup>154</sup> investigated six physicians (three women and three men) at the Vallot Mont Blanc Observatory at an altitude of 4,382 m for 60 hours. Six control volunteers were also studied and tested at sea level at the same times of day as the altitude group. All 12 volunteers were evaluated on a task that involved entering letter sequences with a 9-number keypad like that on a computer keyboard. The pairing of letters with the keys was defined for each trial and indicated with a diagram, spatially analogous to the keypad, that showed a letter on each key. A five-letter sequence that was to be entered on the keypad was also indicated on the diagram. Character-entry performance under these conditions was scored with a derived index that incorporated both the speed and the accuracy of performance. After 8 to 20 hours at high altitude, a measure of performance on the data-entry task that combined both speed and accuracy was less than control values; after 48 to 60 hours at high altitude, performance recovered to sea-level values.

Fine and Kobrick<sup>155</sup> reported that they found increased errors during exposure to hypoxia on tasks

such as receiving information from radio transmissions. Tichauer<sup>124</sup> found that even fully acclimatized personnel working in machine shops at 4,120 m committed more errors and required more time to produce bicycle axles than personnel at lower altitudes. Varied performance outcomes are common, since the characteristics of the task influence the quality of performance and number and types of errors.<sup>145</sup> For example, errors are more likely to occur when tasks are paced by external conditions such as an assembly line or receiving radio transmissions that cannot be "said again." When the pace of the task is set by the subject under stressful conditions (eg, cognitive tasks administered via paper and pencil), response rates are likely to be sacrificed for low error rates. A slowed-processing model in the scientific literature incorporates conditions such as altitude exposure, aging,<sup>156</sup> and nitrogen narcosis.<sup>157</sup>

### Correlations Between Measured Effects

Shukitt-Hale, Banderet, and Lieberman<sup>44</sup> conducted a study to determine whether individuals afflicted with initial symptoms of AMS would be more susceptible to adverse changes in other symptoms, mood states, and performance. The AMS-Cerebral (AMS-C) factor of the Environmental Symptoms Questionnaire was chosen as a measure of altitude sickness because it is a commonly used standard index of the degree of illness. Thirty-eight other measures were chosen to assess various symptoms, moods, and performance. Volunteers were evaluated after exposure to 4,700 m for 5 to 7 hours on 11 symptom, 13 mood, and 14 cognitive-motor performance measures.<sup>44,45</sup> The AMS-C scores were significantly correlated with composite measures of symptoms ( $r = 0.90$ ), moods ( $r = 0.77$ ), and performance ( $r = 0.59$ ). After 5 to 7 hours at 4,700 m, the measure of mountain sickness (AMS-C) was most like (ie, most associated with) other symptoms seen at altitude. This measure of mountain sickness was less like adverse mood changes and least like measures of impaired cognitive performances. One reason why the different magnitudes of correlations with composite measures of symptoms, moods, and performance result is because the time courses of these measures are different. Therefore, it is important to measure a variety of parameters during altitude studies so that the varied changes can be characterized.

In a study by Crowley and colleagues,<sup>158</sup> soldiers ascended to a simulated altitude of 4,300 m and remained there for 2.5 days. A test battery consisting of nine cognitive tests, a mood scale, and an AMS questionnaire was administered four times daily.

Transient deficits in cognitive performance occurred on day 1 (code substitution, Stroop test, and logical reasoning). Moods of volunteers who were ill with AMS were more negative and their performance improved less than volunteers with lesser illness. The researchers concluded that after rapid ascent (10 min) to 4,300 m, performance is most affected during the first 8 hours; the performance of individuals affected by AMS improves more slowly; and these afflicted individuals have more negative moods than those who feel well.

Regard and colleagues<sup>159</sup> showed that rapid ascent to 4,559 m within 24 hours had small, but different, effects on cognitive performance, depending on the later development of AMS. Climbers who developed

AMS within a 24- to 48-hour stay at high altitude were mildly impaired in short-term memory but improved in conceptual tasks. Climbers who remained healthy had better short-term memory performance but no improvement in cognitive flexibility.

The relationship between psychological factors and AMS was explored in another study.<sup>160</sup> Individuals susceptible to AMS were significantly more anxious (both in trait anxiety and state anxiety before final ascent) than those who were not. Therefore, anxiety appears to be a good psychological predictor of AMS, although it is unknown if it is the cause or a correlate. Anxiety-reducing methods such as relaxation training and self-hypnosis may be used to prepare susceptible climbers before expeditions.

### **COPING WITH HIGH TERRESTRIAL ELEVATION AND MINIMIZING ADVERSE EFFECTS**

Earlier in this chapter, we emphasized that most adverse changes occur in symptoms, moods, and cognitive and psychomotor performances after ascent to altitudes higher than 3,000 m. Treatments to minimize these adverse effects include psychological, operational, and medical strategies. Psychological strategies often involve training and familiarization with the adverse effects that will be experienced at HTE. Learned compensatory practices and behaviors, together with greater tolerance of unpleasant situations, help military personnel cope better with adverse effects.<sup>161,162</sup> Much military training is designed with such objectives and outcomes in mind. Operational strategies include staging at intermediate altitudes, acclimatizing, and using supplemental oxygen from tanks or oxygen generators. Lastly, medical strategies often involve use of medications.

In addition, new strategies need to be developed that are more effective and better suited to varied deployment requirements for HTE. Laboratory work with small animals suggests that a neurochemical approach may be promising for reducing adverse behavioral changes at HTE; in the future, adverse performance and mood changes in humans may be controlled by altering neurochemistry.

This section describes the characteristics, limitations, and potential benefits of these strategies for minimizing the adverse effects of HTE, as well as some of the medical contraindications and complicating factors. In many situations in the field, the beneficial strategies discussed are employed together.

#### **Psychological Strategies**

The fact that we can live, work, and play in adverse environments testifies to our adaptive capa-

bilities.<sup>163</sup> Physiological compensations greatly facilitate coping with adverse conditions and are the most important. For example, the body changes the amount of blood flowing to the brain to compensate for the availability of oxygen and the brain's requirements for oxygen. Cerebral blood flow during rest is 700 to 750 mL/min at sea level; at 5,800 m, it may be almost doubled; and at 7,600 m, it may be increased 4-fold.<sup>8</sup> But psychological adaptations and strategies are also critical,<sup>15,42</sup> as they can facilitate coping and functioning in high-altitude environments.<sup>72,164</sup> In a hiking or climbing party, reassurance to the afflicted person can have a beneficial effect on reducing the symptoms of AMS and the discomforts at high altitude.<sup>15</sup> This observation suggests the importance of social and interpersonal variables in influencing reactions to symptoms and discomfort.<sup>161</sup> Reassurance and time can do much to hasten acclimatization to a more challenging, high-altitude environment.

A study<sup>165</sup> of Army personnel showed that the more the soldiers expected to dislike the environmental conditions, the more tense, depressed, angry, fatigued, and physically uncomfortable they were during cold weather training at moderate altitudes. Experience in stressful environments makes cognitive performance more robust because of adaptive changes in behavioral arousal, attentional capacity, or controlled versus automatic processing of the task.<sup>157,163,166</sup> Involvement in a performance task during high-altitude exposure apparently decreases the types and intensities of discomforts reported.<sup>167</sup> Experiencing the symptoms and discomforts of a stressful environment will facilitate subsequent coping in similar situations.<sup>157,161-163,168</sup> If people are aware of the nature and time course of altitude effects, they



can devote extra attention to tasks, create checks for errors, manage personnel to ensure redundancy of procedures during critical times, and develop other compensatory strategies.<sup>47,167,169</sup>

### Operational Strategies

Prolonged stay at HTE results in physiological acclimatization, which produces adaptive effects on oxygen delivery and regulation of metabolites.<sup>72,150,170,171</sup> Beneficial effects occur within days to weeks, depending on the altitude, rate of ascent, and the dependent measures chosen for evaluation. With enough time at altitude, there is usually a dramatic reduction in symptoms, adverse moods, and behavioral impairments. Lyons and colleagues<sup>172</sup> demonstrated that after acclimation (16 d continuously at 4,300 m altitude), six male volunteers experienced few symptoms of AMS when they were exposed again to 4,300 m, even after living at sea level for 8 days.

Acclimatization can be induced in many ways. Mountain climbers and others use the strategy of slow ascent to high altitude, providing time for acclimatization and symptoms to subside.<sup>1,3,4,6,7,150,173,174</sup> A leaflet by the Himalayan Rescue Association emphasized this strategy for trekkers proceeding above 3,658 m: "The golden rule: Don't go 'too fast too high.'"<sup>15(p153)</sup> Others try staging, where people stay at one altitude for a few days before ascending farther.<sup>27,85,150</sup> However, wearing a rebreathing device at sea level that produced hypoxic breathing at altitude was not found to be beneficial.<sup>175</sup>

As described above, another strategy was evaluated in personnel who worked in observatories at 4,200 m.<sup>63</sup> Some lived and slept at low altitude but drove to the top to work. Personnel with intermittent exposures to high altitude experienced AMS symptoms for more days than personnel who stayed on the mountain continuously.

Supplemental oxygen reduces or defers most effects of high altitude. Pilots in high-performance fighter aircraft use it, as do some mountain climbers.<sup>1,3,134</sup> Its main limitations are logistical (ie, the weight, bulk, and difficulty of transporting it) but the Gamow Bag (US distributor: Chinook Medical Gear, Inc, Durango, Colo), a large 6.6-kg, inflatable nylon bag with an air-tight zipper, and the Certec (a French product) offer promise to individuals who are severely afflicted with altitude disorders.<sup>15,176-179</sup> An important feature of these inventions is that, by encapsulating an individual and introducing ambient air under modest pressure into the bag, lower altitudes and greater barometric pressures are created, thereby obviating the necessity of transporting heavy, bulky oxy-

gen tanks up the mountain and usually making the transporting down of stricken climbers less urgent.

In some work situations, it may be advantageous to add supplemental oxygen to the ambient environment or administer it through a nasal clip or facial mask.<sup>14,180</sup> For example, a telescope technician who arrives from sea level by car to provide repairs to an inoperative telescope may well provide the highly critical and necessary support on the observatory in less than an hour and then return to sea level. Daily shift workers at an observatory often drive to work, work their shift, and then return to low altitude.<sup>63</sup> If supplemental oxygen was provided at the observatory, the well-being and functioning of personnel could be sustained as it is at sea level.<sup>14</sup> West<sup>180</sup> demonstrated that increasing the oxygen concentration from 21% to 25% at high altitudes of 4,000 to 5,500 m reduced the effective altitude by 1,500 m. An increased hazard of fire was not a real concern because under these conditions of reduced atmospheric pressure, items burned less readily than they would have at sea level.<sup>180</sup>

### Medical Strategies

Some medications improve functioning at high altitude; others do not. Acetazolamide, the current medication of choice,<sup>3,15,149,150,174,181-183</sup> enables most personnel to work and function at high altitude with less time devoted to acclimatization.<sup>15</sup> Acetazolamide is a carbonic anhydrase inhibitor; it stimulates ventilation and partially corrects acid-base and gas-exchange imbalances in the blood without impairing cognitive performance.<sup>184</sup> It increases  $\text{PaO}_2$  at high altitude,<sup>83</sup> improves sleep and reduces symptoms of hypoxia,<sup>185</sup> and ameliorates adverse moods.<sup>26</sup> Acetazolamide reduces symptoms best when combined with staging.<sup>27</sup>

Dexamethasone, a powerful anabolic steroid, is even more effective than acetazolamide.<sup>15,174,186-188</sup> It reduces performance impairments and adverse moods without significant psychological effects.<sup>189</sup> The drug is best used with caution, however, because it may have physical side effects.<sup>3,190,191</sup>

Tyrosine, a precursor of the neurotransmitter norepinephrine, reduces some of the adverse effects of high altitude and cold.<sup>129,192-194</sup> Tyrosine improved symptoms, moods, and various performances in volunteers who showed average or greater than average adverse effects during an environmental challenge in which they had been treated with a placebo.<sup>129,192,193</sup>

The drugs furosemide,<sup>150</sup> phenytoin,<sup>195,196</sup> and naproxen,<sup>197</sup> are ineffective or possibly harmful. Sleep preparations, alcohol, and sedatives should be

avoided.<sup>15</sup> Stimulants may increase the symptoms of AMS and impair performances that require subtle discriminations or judgments. Common antacid tablets did not reduce altitude effects<sup>198</sup>; this finding is consistent with earlier data from others.<sup>150</sup> Supplemental intake of potassium is contraindicated.<sup>72</sup>

Climbing or driving to high altitudes, and even flying in aircraft (pressurized or nonpressurized), can result in decompression sickness if a person experiences reduced atmospheric pressures too soon after he or she has scuba dived. In addition to Navy divers or SEALs, such concerns may be relevant for other military personnel who perform parachute and free-fall jumps from high altitudes. The article "Medical Guidelines for Air Travel"<sup>199</sup> specifies the minimum interval between diving and flying in pressurized commercial aircraft (pressure equivalent to ~ 3,000 m). Twelve hours is considered sufficient after one dive per day. If diving occurred more than once per day or was performed over several days, then more than 12 hours should

elapse between the last dive and flying.

"Medical Guidelines for Air Travel"<sup>199</sup> also describes medical disorders (eg, cardiovascular and pulmonary disease) that may complicate flight in an aircraft or balloon. These diseases may also compromise climbing and functioning at high altitude. Such concerns are supported by empirical data. For example, 24 patients with known ischemic heart disease were evacuated with military aircraft; cabin pressure was maintained at 2,100 m; during flight, the average saturation of oxygen in the blood was 94.5%.<sup>200</sup> Although these data do not indicate a life-threatening or critical level of oxygen desaturation, they suggest that people with such medical conditions may be at greater risk in commercial aircraft or at high altitude because hypoxemia even in a partially pressurized aircraft can be potentiated by their preexisting disorders. Military personnel and civilians planning to climb or work at high altitude should be medically evaluated to ensure that they are healthy enough to deal with the specific challenges of exposure to HTE.

## SUMMARY

Cognitive and psychomotor performance and mood states, including many critical behavioral functions such as sleep, memory, reasoning, and vigilance, are significantly impaired by ascent to HTE higher than 3,000 m. Impairments in behavior caused by HTE can degrade military operations because the judgment and rate and accuracy of performance of military personnel can be affected. Such adverse effects have distinct and measurable time courses; onset of some effects is immediate (cognitive performance), whereas the onset of others is delayed (symptoms of AMS or adverse moods). The behavioral consequences of HTE are primarily dependent on the level of altitude, the duration of exposure, the rate of ascent, an individual's state of physiological acclimation or acclimatization, characteristics of the task performed, and characteristics of the individual such as hypoxic sensitivity.

Military history documents that the adverse effects induced by HTE need to be considered when military operations at altitude are planned and un-

dertaken. Current research indicates that some performance decrements induced by ascent to extremely high mountains (eg, Mount Everest, 8,848 m) may persist for a year or longer after return to lower elevations.

Psychological, operational, and medical strategies have been employed to minimize these adverse effects. Psychological strategies often involve training and familiarization with the adverse effects that will be experienced at high altitude. Operational strategies include staging at intermediate altitudes, acclimatizing, and using supplemental oxygen from tanks or oxygen generators. Medical strategies often involve the use of medications to improve functioning at altitude and techniques to avoid complications.

In most situations, multiple strategies are employed. The strategies now available and new developments to come will ensure that high-altitude military operations in the future will be less affected by adverse changes in cognitive and psychomotor performance and mood.

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